PEPTIC ULCER

Diagnosis and Treatment

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by CLIFFORD J BARBORKA
MD MS DS FACP
Associate Professor of Medicine and Chief Gastro intestinal Clinics Northwestern University Medical School Attending Physician Passavant Memorial Hospital Senior Consultant in Gastroenterology Veterans Administration Research Hospital Chicago Illinois formerly Consulting Physician Mayo Clinic

and E CLINTON TEXTER JR MD
Associate in Medicine and Assistant Chief Gastro intestinal Clinics Northwestern University Medical School Attending Physician Passavant Memorial Hospital Attending in Gastroenterology Veterans Administration Research Hospital Chicago Illinois

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This book is dedicated to those physicians who are engaged in the general practice of medicine

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PREFACE

The practicing physician is constantly being engulfed by a flood of medical literature Literature on peptic ulcer is no exception There are excellent books directed toward the research worker the gastroenterologist and the surgeon We feel there is a need for a practical concise handbook to which the practicing physician can turn for information and guidance in the treatment and management of the ulcer patient

This is such a book written out of our experience and incorporating as well current opinions regarding the medical and surgical treatment of peptic ulcer and its complications Since sound treatment rests upon firm knowledge of etiology and pathogenesis these subjects are covered Alterations in the normal physiology of the gastrointestinal tract must be understood if proper measures are to be taken to correct the conditions existing in disease

The diagnostic methods are discussed along with the newer concepts of treatment An attempt has been made to delineate the values and limitations of both medical and surgical treatment A rational approach to the gastric ulcer problem is presented It is our firm conviction that the importance of the patient physician relation in the modern management of peptic ulcer cannot be overemphasized The

manuscript and illustrations We are indebted to Miss Madge Walsh for her assistance in preparing the figures and photographs to our secretary Miss Catherine M Lundy and our technician Miss Junko Ikeya for their untiring efforts in the preparation of the manuscript and to Miss Wanda T Langum Assistant Administrative Dietician at Passavant Memorial Hospital We should also like to acknowledge the splendid co operation of Mr Theodore A Phillips of Little Brown and Company

CLIFFORD J BARBORKA M D
E CLINTON TEXTER, JR M D

Chicago Illinois
April 1955

benefits of medical treatment are enhanced by the physicians ability to encourage the willing and energetic co operation of his patient *Education is necessary for the patient to understand the fact that the disease is controlled rather than cured and thereby long term therapy is improved* It is important for the patient not to mistake remission for cure The patient must be impressed with the necessity of continuing on a prescribed regimen during symptom free periods Most patients will co operate willingly if they are helped to understand that adherence to their dietary and therapeutic regimens will not alone keep them free of symptoms in most instances but will be a definite aid in preventing recurrences

Therefore our discussion is constantly directed toward helping the practicing physician in his efforts to receive the full co operation of his patient The organization of the book is such that each chapter can be read almost as an independent essay on a particular facet of peptic ulcer with a review of the general problem of gastric ulcer in the final chapter Much of the material will be intelligible to the educated patient and thereby serve as a guide to him in his own management under the direction of his physician Every physician is aware that the peptic ulcer patient must learn not only to live with his ulcer" but to live with himself

We are indebted to the foundations private individuals and pharmaceutical manufacturers who have supported our studies and made continued research at Northwestern University Medical School possible We should like to express our appreciation also to Hubbard W Smith M D our research fellow for his valuable assistance in compiling the

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INTRODUCTION

Peptic ulcer appears to have had its beginnings with man s occupation of this planet Ancient writings dating from the time of Aesculapius and Celsus mention the occurrence of ulcer and even make some suggestions for its treatment Many famous people have been afflicted with peptic ulcer It is probable that the well known stance of Napoleon Bonaparte was due to his attempt to get relief from his ulcer distress It was thought that he had gastric carcinoma but careful studies have shown that he had a chronic peptic ulcer which had perforated and walled off

The first ulcers that were recognized clinically were those that perforated Most of these were gastric ulcers Duodenal ulcers began to be recognized about the middle of the nineteenth century About the same time attempts were made to treat ulcers by dietary measures The French clinicians proposed the use of milk and eggs in the treatment of peptic ulcer Subsequently there was a period when starvation was used in the erroneous belief that it would rest the stomach Fenwick in 1868 stressed the importance of small bland feedings for the ulcer patient and the use of sodium bicarbonate to control acidity However little attention was paid to the dietary treatment of ulcer until 1915 when

Sippy again re emphasized the necessity for a strict pro gressive bland diet along with massive alkalinization This was followed by the work of Meulengracht [3] who demon strated the value of early feeding in the treatment of bleed ing duodenal ulcer

Advances in our diagnostic ability were made at the same time Cruveilhier [4] carried out classic studies on the patho logic changes of peptic ulcer Pathologists subsequently began to recognize peptic ulcer with increasing frequency It was not until 1895 when Roentgen discovered x rays that the widespread nature of peptic ulcer disease became known In 1898 Cannon showed that the gastrointestinal tract could be visualized and in the succeeding fifty five years rapid advances have been made in this diagnostic technique

The first surgery for peptic ulcer was carried out in the 1880s Following the demonstration that surgery could be carried out safely great strides were made both in Europe and in the United States With succeeding years the opera tions of gastroenterostomy gastric resection and more re cently vagotomy along with gastroenterostomy have been advocated for the treatment of patients with complicated ulcers The American Gastroenterological Association has recently completed a monumental task of evaluating these operations Its findings along with other studies should be of great value in helping the practitioner to decide what surgery should be employed in the individual case

Peptic ulcer is a common condition affecting an estimated 10 per cent of the worlds population It is also said to be the twelfth most costly disease in terms of disability All ages are affected although it tends to be most common in

the middle years and less common at the extremes of life There is a sex predilection males being affected approximately four times as often as females The most common site for peptic ulcer is the first portion of the duodenum When diagnosed by x ray duodenal ulcer is approximately nine times as common as gastric ulcer It is probable however that gastric ulcer is more common than these statistics would indicate as at autopsy the incidence of the two lesions is identical This discrepancy is probably explained by the fact that many gastric ulcers present such bizarre symptoms that they are not diagnosed clinically and subsequently heal without ever having been recognized Ulcers can also occur in other parts of the gastrointestinal tract bathed by gastric acid including the esophagus and the jejunum after short circuiting types of operations

A specific cause for ulcer is not known but it is generally held that ulcer falls into the category of psychosomatic diseases Stress is probably an important etiologic factor and there have been attempts to relate it to the adaptation syndrome of Selye It has been observed that ulcer occurs most frequently in nervous high strung persons Both heredity and constitutional factors have been studied but these are not considered of great significance in the genesis of ulcer Circulatory factors may play some role It is probable that they are not too important

The pathologic changes in ulcer consist of a localized loss of the lining mucosa which is usually single but may be multiple This ulcerated area is usually surrounded by inflammatory changes with some evidence of necrosis and ultimately scarring

The symptoms in ulcer patients are generally fairly char

acteristic Pain or distress which occurs on an empty stomach and is usually relieved by taking food is typical This pain may follow each meal may wake the patient at night tends to be present for several days at a time and frequently is absent for long periods The symptoms of gastric ulcer are not as characteristic as those of duodenal ulcer and when complications develop the symptoms frequently become difficult to interpret

Physical examination of the patient is not of much help in establishing the diagnosis of peptic ulcer Tenderness may be present on palpation over the upper abdomen but physical signs are not striking in patients with uncomplicated ulcers The diagnosis is usually established in patients with characteristic symptoms by the x ray demonstration of a crater or by second ry x ray signs of ulceration Examination of the interior of the stomach by gastroscopy may also be of assistance in demonstrating the presence of gastric ulcers

The differential diagnosis of peptic ulcer may be difficult The stomach and first portion of the small bowel lie in close proximity to the gallbladder pancreas and kidney and are just beneath the heart and lungs It is a common observation that peptic ulcer can simulate cardiac disease gallbladder colic and pancreatitis There is also the ever present problem of differentiating gastric ulcer from ulcerating cancer of the stomach

The therapy of peptic ulcer is primarily medical It is estimated that about 90 per cent of patients require only medical care while the remaining 10 per cent may ultimately require surgical treatment The basic principles of treatment — rest a bland diet with frequent feedings and the

use of antacids sedation and antispasmodics — are well known These basic principles have not changed significantly in the last thirty years

Recently the new synthetic quaternary amine compounds having anticholinergic activity have been added to our armamentarium and they possess certain advantages not present in the belladonna atropine group of antispasmodics The treatment of peptic ulcer is certainly not perfect and despite the addition of anticholinergic drugs little progress has been made toward the goal of preventing recurrences or producing permanent cures

For those people who fail to respond to medical management the so called intractable ulcer patients or for those patients who develop complications surgery is necessary Several procedures have been devised and advocated Although surgical treatment must be individualized in every instance considerable progress has been made in recent years in clarifying the indications and value of the several operations It is hoped that with continuing research better treatment can be devised for patients with peptic ulcer

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ANATOMY AND PHYSIOLOGY

A discussion of the anatomy of the stomach and duodenum might seem out of place in a handbook devoted to peptic ulcer Actually it is not inasmuch as knowledge of the anatomy blood supply and innervation of the stomach and duodenum is fundamental to an understanding of the basic features of the disease Such an understanding is also important in evaluating the various methods which have been employed to treat peptic ulcer Knowledge of the basic physiologic processes of gastric secretion and motility is as important as if not more important than knowledge of the anatomic features Peptic ulcer results from an alteration in normal physiology An understanding of the normal physiology is essential to an understanding of the abnormal

ANATOMY

Gross Anatomy of the Stomach

The stomach lies below the left diaphragm and is continuous with the esophagus above and the duodenum below It is the most dilated part of the digestive tract Its

size and shape are variable depending upon the build of the person the contents of the stomach and the position of adjacent organs Its capacity is approximately 1 quart

The upper end of the stomach the cardiac orifice is located opposite the eleventh thoracic vertebra The pyloric orifice which connects the stomach and duodenum lies to the right of the midline at the level of the first lumbar vertebra The lesser curvature of the stomach extends between the cardiac and pyloric orifices and forms the right border of the stomach The greater curvature also begins at the cardiac orifice and is about four times as long as the lesser curvature From the cardiac orifice the greater curvature extends upward to the left forming the superior margin of the stomach The highest point is at the level of the sixth left costal cartilage From this point the greater curvature courses downward forward and to the right ending at the pylorus The stomach has an anterior and a posterior wall On the left the anterior wall is adjacent to the diaphragm on the right it is in contact with the left lobe of the liver and the anterior abdominal wall The posterior wall is in contact with the diaphragm spleen left adrenal gland left kidney pancreas left colic flexure and transverse mesocolon

The upper portion of the stomach is separated from the esophagus by a muscular valve the cardiac sphincter The cavity of the stomach is divided into three parts The portion of the stomach lying just under the diaphragm and just under the cardiac orifice is called the cardia or fundus The major portion of the stomach the body or corpus extends from the level of the cardiac orifice to the antrum

The antrum is the portion of the cavity of the stomach lying distal to the angulus or muscularis sphincter antri On gastroscopic examination the muscularis sphincter antri can be seen as a muscular curtain like structure which partially divides the body of the stomach from the antrum The angulus on the interior of the stomach corresponds to the incisura angularis on the exterior of the stomach The incisura angularis is that point where the lesser curvature changes abruptly from a downward course to an upward one towards the pylorus The cavity of the distal stomach is separated from the duodenum by the pyloric sphincter

There is still some confusion regarding the anatomical terminology of the distal stomach Russell *et al*[1] have suggested that the term pylorus be limited to the pyloric channel the adjacent stomach being termed the antrum and the distal half of the antrum the prepyloric area

Microscopic Anatomy of the Stomach

The wall of the stomach consists of four coats an outer smooth serosal layer a muscular layer the submucosa or glandular layer and an inner lining or mucosal layer The serosa consists of connective tissue covered by peritoneum in which course the nerves and blood vessels which supply the stomach The muscular layer comprises three layers of smooth muscle an outer longitudinal a middle circular and an inner oblique layer The submucosa consists of loose areolar tissue containing fat cells a plexus of nerves and blood vessels The mucous layer is divided into the muscularis mucosae the tunica propria and epithelium The gastric epithelium is a single layer of columnar cells containing mucus

Gross Anatomy of the Duodenum

The duodenum is the first portion of the small intestine It measures 25 cm in length It has no mesentery and is covered in part with peritoneum It occupies a circular course enclosing the head of the pancreas (Fig 1)

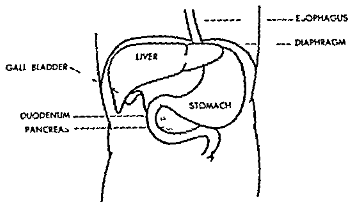


FIGURE 1

Schematic diagram of the anatomy of the esophagus stomach and duodenum

The duodenum is divided into four parts The first portion which includes the duodenal bulb is directed upward and to the right beneath the liver and the gallbladder and anterior to the gastroduodenal artery the bile duct and the portal vein The descending or second portion covers the medial portion of the right kidney and lies behind the transverse colon The bile and pancreatic ducts empty into this portion At the level of the fourth lumbar vertebra the third portion of the duodenum angles to pass across the inferior vena cava The duodenum angles again to pass anterior to

the aorta and upward where it becomes the jejunum The blood supply is derived from the right gastric artery and the *superior and inferior pancreaticoduodenal arteries*

Microscopic Anatomy of the Duodenum

The walls of the duodenum like those of the stomach consist of four layers There is an outer serosal layer a muscular layer a submucosal layer and a mucosal layer The submucosa contains Brunner s glands which secrete alkaline mucus The mucosa of the duodenum is columnar epithelium

Innervation of the Stomach and Duodenum

The stomach is supplied with extrinsic nerve fibers from both branches of the autonomic nervous system The vagus nerves supply the parasympathetic innervation while the sympathetic nerves come by way of the splanchnic nerves In addition the stomach has intrinsic innervation within the layers of its wall

The vagi or tenth cranial nerves have their origin in the brain stem and reach the stomach by way of the mediastinum After giving off branches which supply the heart and lungs they form two main branches which course along the outside of the esophagus passing through the esophageal hiatus to supply the stomach The right or posterior branch sends fibers to the posterior portion of the stomach and the left or anterior branch supplies the anterior surface and lesser curvature of the stomach and the first portion of the duodenum Both the anterior and posterior branches divide almost immediately on passing through the esophageal hiatus into a fine network In addi

tion to the main branches small twigs are given off above this level This is of considerable importance in relation to the recently revived operation of vagotomy Many anatomists have claimed that it is impossible to perform a complete vagotomy or vagectomy from the infradiaphragmatic approach and that such an operation is possible only by the transthoracic route Nonetheless the transthoracic route has been abandoned in preference to the infradiaphragmatic section of the vagus nerves This anatomical arrangement undoubtedly explains some of the therapeutic failures following vagotomy inasmuch as the vagus nerves have not been completely severed

The sympathetic nerves to the stomach and duodenum are derived from the sixth seventh eighth and ninth thoracic spinal nerve roots and travel to the stomach and adjacent organs via the splanchnic nerves The splanchnic nerves carry sympathetic fibers which control the motor functions of the stomach and also visceral afferents which conduct sensations arising from the stomach and duodenum

It was thought in the past that the vagus nerves served primarily to stimulate the motor function of the stomach and that the sympathetic nerves were inhibitory but this is not entirely correct It is best to think of these two nerve supplies as constituting dual mechanisms whereby nerve impulses serve to modify the reactivity of the local neuromuscular mechanisms within the stomach itself

Visceral sensation is transmitted to the brain by visceral afferent fibers No visceral sensations are produced by many of the usual stimuli including cutting burning and crushing Tension resulting from distention of the lumen of a hollow viscus or muscle spasm produces pain The stomach

is relatively insensitive to heat and cold but gross changes in temperature can be recognized

The visceral afferent fibers pass uninterruptedly through the celiac plexus to form the greater lesser and least splanchnic nerves These fibers pass without a synapse through the sympathetic trunk and white rami communicantes to the spinal nerve root where the corresponding ganglia cells are This arrangement differs from that of the sympathetic efferent nerves which have a preganglionic fiber a ganglion and a postganglionic fiber Thus with the use of ganglionic blocking agents one can blockade the efferent nerves but the visceral afferent or sensory fibers are left unaffected

Gastric sensation remains intact following section of the vagus nerves although the cephalic phase of gastric secretion is abolished Resection of the splanchnic nerves abolishes pain of visceral origin Thus pain arising from an uncomplicated ulcer would not be recognized by the patient following splanchnicectomy although pain of parietal origin secondary to peritonitis resulting from a perforation could be Because splanchnicectomy is not infrequently performed on patients with hypertension this is of considerable importance Hypertension and peptic ulcer are commonly associated and some of the patients in which this association occurs have difficulties with their ulcers following splanchnicectomy because the usual ulcer pain symptoms are abolished

Blood Supply of the Stomach

The stomach has a copious supply of blood which is closely related to the motor and secretory activities of the

stomach The anatomical arrangement of the larger vessels is important when one is considering what type of surgery is to be carried out The relation to the blood supply may determine the risk of hemorrhage There is also the possible relation of vascular supply to the formation of ulcer and to ulcer pain

The blood supply of the stomach is derived from the celiac axis The left gastric artery joins the stomach near the cardia and continues along the lesser curvature of the stomach The right gastric artery which is usually derived from the hepatic artery reaches the stomach near the pylorus supplying the anterior and posterior surfaces in this area The right gastroepiploic artery which is derived from the gastroduodenal artery appears just below the pylorus and passes along the greater curvature in this area The left gastroepiploic artery is similarly disposed along the greater curvature of the body of the stomach The greater curvature of the fundus receives its blood supply from the short gastric branches of the splenic artery (Fig 2) These arteries join to form a network of vessels which is sufficient to prevent necrosis of the stomach even though all but one vessel are tied It can easily be seen therefore why it is difficult to stop hemorrhage from a gastric ulcer by ligating the extrinsic vessels in the region of the ulcer

It can be demonstrated by gastroscopic examination that the vascularity of the mucosa is subject to changes which are related to influences of psychic origin There is also evidence that a shunt mechanism may operate within the stomach so that at times the blood is diverted from the stomach into arteriovenous shunts while at other times it is funneled through the complete capillary bed These

shunts have been demonstrated by microarteriography The arteries of the stomach were injected with a radio opaque fluid of small particle size microscopic sections were cut and radiographs were made of microscopic sections

Little is known of the blood flow of the stomach Total

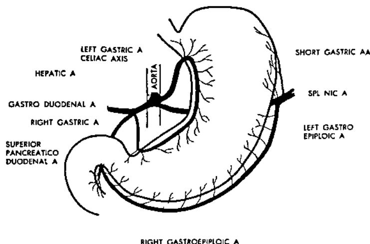


FIGURE 2

Schematic diagram of the arterial blood supply of the stomach and duodenum

splanchnic blood flow can be measured but there is no way as yet to determine what proportion of splanchnic blood flow goes through the stomach Experimental techniques for measuring gastric blood flow are being studied at the present time

The blood supply of the stomach is related to the location of ulcers It has been shown that ulcers both in the stomach and in the duodenum tend to be located in the

areas which are least vascular Furthermore in the production of experimental ulcers in animals it has been shown that a decrease in blood supply is generally necessary before an ulcer develops It appears likely that similar factors operate in man

GASTRIC SECRETION

An imbalance between the eroding or destructive factors in gastric secretion and the defense factors is considered important in the development of an ulcer This balance may be disturbed in several ways There can be an increase in the quantity or duration of the secretion of the hydrochloric acid–pepsin combination There can be a decrease in the secretion of the buffering fluids which neutralize and inactivate the hydrochloric acid–pepsin combination and lastly there can be a decrease in the resistance of the local tissues to the action of the erosive hydrochloric acid–pepsin In order to understand the factors underlying this imbalance it is essential to know what the normal mechanism of gastric secretion is

Two portions of the stomach are concerned with gastric secretion The proximal two thirds of the stomach contains millions of tubular glands whose function is to produce the active digestive elements of gastric juice namely pepsin and hydrochloric acid Pepsin the digestive enzyme is formed by the chief cells which are located in the body of the gland while hydrochloric acid is formed by the parietal cells The surface epithelial cells secrete mucus The distal third of the stomach contains the pyloric glands whose chief function is the formation of mucus (Fig 3)

Components of Gastric Secretion

HYDROCHLORIC ACID The complete details of the mechanism of secretion of hydrochloric acid are not entirely clear It is known that the main constituents water carbon diox

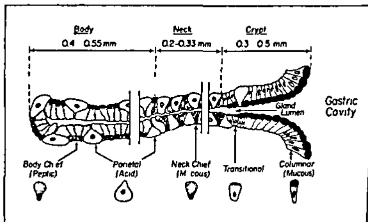


FIGURE 3

Cross section of a gastric gland (From Barborka *et al*[3] Reproduced with kind permission of the editor of the *Quarterly Bulletin Northwestern University Medical School*)

ide and chlorides are derived from the blood It is probable that water furnishes the source for the hydrogen of hydrochloric acid Hollander[4] has proposed the "membrane hydrolysis" theory which postulates that the canalicular wall has a selective nonreciprocal permeability which allows only water with hydrogen and chloride ions to pass through it into the lumen of the gland Bicarbonate is returned to the blood

Davenport has shown that carbonic anhydrase an en

zyme which catalyzes the reaction of carbon dioxide and water to form carbonic acid and its ionic breakdown is present in high concentration in the parietal cells The carbonic anhydrase serves primarily to maintain ionic and isotonic equilibrium within the parietal cell It participates in the reverse chloride shift wherein chloride is secreted in exchange for bicarbonate It appears that carbonic anhydrase furnishes one source of hydrogen ions for hydrochloric acid This is supported by the observation that the administration of carbonic anhydrase inhibitors such as acetazoleamide may markedly inhibit the production of hydrochloric acid [6, 7]

It has been postulated by Conway [8] and others [9, 10] that the hydrogen is concentrated by a series of steps employing a so called "redox cycle (Fig 4)

Pure parietal secretion contains 166 milliequivalents per liter of chloride 159 of hydrogen ion and 7 of potassium ion This solution is isosmotic with blood Gastric juice does not reach this concentration because nonparietal secretion neutralizes and dilutes the parietal secretion High concentrations of acids have been observed up to 110 clinical units (a clinical unit being equal to 1 milliequivalent per liter) and under strong stimulation the acid concentration of gastric juice may reach as high as 150 milliequivalents per liter

PEPSIN Pepsinogen a protein is formed by the chief cells and is converted to pepsin in an acid medium (below pH 6) The optimum pH for the proteolytic activity of pepsin is about pH 2 Stimulation of the vagus nerve produces an increase in secretion of gastric juice which contains mucus and is high in peptic activity Stimulation with

histamine on the other hand yields a highly acid secretion which is low in peptic activity and practically mucus free

MUCUS Gastric mucus is secreted by the surface epi

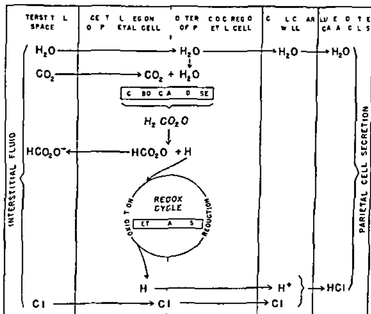


FIGURE 4

Schematic diagram of the redox concept of gastric secretion according to Conway (From Texter and Barborka Reproduced with kind permission of the editor of *Gastroenterology*)

thelial cells by the chief cells of the neck of the fundic glands by the pyloric gland cells and by the cardiac gland cells There are two components of mucus in the fundus and body of the stomach The first of these is a layer of viscid mucus which covers the inner wall of the gastric cavity and the second is a layer of tall columnar cells im

mediately beneath this sheet of mucus together with low columnar and cuboidal cells which line the crypts of the gastric glands[11] Several components have been isolated from gastric mucus including two types of mucopolysaccharides Gastric mucus exists in two physical forms dissolved mucus and visible mucus Its function is to coat the mucosa of the stomach protecting it from erosion It also inhibits pepsin and neutralizes hydrochloric acid

Mechanisms of Gastric Secretion

The secretion of gastric juice and hydrochloric acid is usually divided into two phases interdigestive secretion and digestive secretion

INTERDIGESTIVE SECRETION A small amount of gastric juice is secreted by the fasting stomach between periods of digestion Bloomfield[12] has termed this basal secretion and it is this basal secretion which is measured in the one hour basal gastric secretion The mechanism for secretion of hydrochloric acid during the basal phase is unknown although it is possible that hormonal factors influence the secretion

DIGESTIVE SECRETION Gastric secretion in relation to food is divided into three phases the cephalic the gastric and the intestinal The cephalic phase denotes the secretion which arises as a result of a stimulus in the region of the head These include the sight smell taste and thought of food The amount of secretion during this phase is extremely variable The cephalic phase of gastric secretion is abolished following vagotomy

The gastric phase refers to formation of hydrochloric acid as a result of stimuli acting within the stomach Two

types of stimuli are known mechanical stimuli and chemical stimuli Distention of the stomach produces a secretion of acid For this reason it is recommended that ulcer patients not overfill the stomach but instead have small amounts within the stomach nearly all the time The chemical phase of gastric secretion is the result of the action of secretagogues chemical factors which stimulate secretion The most common ones are those present in meat liver and meat extractives Stimulation of gastric secretion results from partial digestion of such foods Because of the enhancement of gastric secretion by secretagogues these foods are excluded from the diet of ulcer patients

Gastric secretion also results from stimuli acting within the intestine The secretagogues which produce gastric secretion when they are in the stomach also stimulate gastric secretion when they are in the intestine Substances such as soaps fatty acids and partially digested protein act as gastric juice secretagogues when within the bowel The volume of gastric juice secreted during these phases is shown below (Ivy *et al*[13])

Phase	*Amount*
Interdigestive	30–60 ml /hr
Cephalic	50–150 ml /20 min
Gastric	225–350 ml /5 hr
Intestinal	200–300 ml /5 hr

HORMONAL INFLUENCE ON SECRETION Gastric secretion is stimulated by the hormone gastrin which is produced by the mucosa of the antrum of the stomach in response to mechanical and chemical stimuli The chemical identity of gastrin is not known Dragstedt *et al*[14] indicate that the antrum plays an important role in gastric secretion in dogs

and that under certain experimental conditions the antrum may greatly increase the output of hydrochloric acid and cause gastroduodenal or gastrojejunal ulcers The role of the antral mechanism in normal human gastric secretion has not been determined There is no conclusive evidence that hyperactivity of the antral secretory mechanism is involved in the gastric secretion which characterizes patients with duodenal ulcer Removal of the antrum in partial gastrectomy is alleged to contribute to decreased gastric secretion following the surgery It has been observed that removal of the antrum during gastric resection for duodenal ulcer does not necessarily decrease the excessive output of acid whereas in contrast vagotomy reduces gastric secretion to approximately normal levels

INHIBITORY FACTORS Gastric secretion as well as gastro intestinal motility may be inhibited by nervous impulses mediated by way of the sympathetic nerves Inhibition of secretion of hydrochloric acid is also observed after administration of fats or sugars when they are present in sufficient concentration This is a result of the action of fats and sugars upon the intestinal mucosa with the production of a hormone which has been termed enterogastrone This natural inhibitory mechanism is made use of in treating ulcer patients Liberal amounts of fat usually in the form of cream are included in such diets This fat stimulates the release of enterogastrone which inhibits hydrochloric acid secretion and also delays gastric emptying

REGULATION OF GASTRIC ACIDITY The formation of gastric acid is regulated by the factors discussed above both those which enhance secretion and those which inhibit it The acidity of the gastric contents is also related to the rate of

types of stimuli are known mechanical stimuli and chemical stimuli Distention of the stomach produces a secretion of acid For this reason it is recommended that ulcer patients not overfill the stomach but instead have small amounts within the stomach nearly all the time The chemical phase of gastric secretion is the result of the action of secretagogues chemical factors which stimulate secretion The most common ones are those present in meat liver and meat extractives Stimulation of gastric secretion results *from partial digestion of such foods Because of the enhancement* of gastric secretion by secretagogues these foods are excluded from the diet of ulcer patients

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stomach give rise to the sensation termed hunger pangs These hunger pangs are peristaltic waves which start in the upper stomach region and pass down to the duodenum

The motor activities of the stomach during digestion can be divided into two types gastric peristalsis and changes in muscle tone Gastric peristalsis consists of regular periodic contractions that segment off the distal end of the stomach and carry the portion of the gastric contents through the pyloric sphincter and into the small bowel In addition to these gross movements smaller changes — called "tone" changes — have been observed within the stomach These consist of a gradual shortening of the muscle fibers of the stomach as the volume of gastric contents decreases

The functions of the stomach during digestion include the reception of the meal mixing of the contents of the stomach and assuring passage of the gastric chyme into the small bowel This is a highly co ordinated function which has been carefully studied by Quigley and his co workers [16] He has observed that the distal portion of the stomach the pylorus and the first portion of the duodenum behave as a co ordinated segment and he has termed this the "antral pump It is his opinion that the pyloric sphincter's chief function is to prevent regurgitation of duodenal contents into the stomach

Several mechanisms operate to prevent any great increase in intragastric pressure when food enters the stomach Initially there is a relaxation of the walls of the stomach and a concomitant inhibition of motor activity The major portion of the food is held in the reservoir or upper portion of the stomach and at periodic intervals portions of the

removal of parietal secretion by emptying of the stomach the ingestion of food or antacids the amount of non parietal or mucous secretion and the amount of secretion extrinsic to the stomach The last factor includes swallowed saliva regurgitated intestinal contents and alkaline bile The amount of acid secretion at the time of a meal depends upon both mechanical and chemical factors concerned with that meal and also with the enthusiasm with which the person ingests the meal It is thought that all patients with free acid form parietal secretion at about the same concentration (approximately 159 clinical units) However during the course of a meal the level of acidity seldom reaches higher than 50 clinical units because of the addition of non parietal secretion and the neutralizing capacity of the ingested food

DUODENAL SECRETION

The duodenum is supplied with Brunners glands which resemble histologically the pyloric glands of the distal stomach The secretion from these glands is a thin alkaline mucous secretion which is capable of neutralizing a significant amount of gastric hydrochloric acid The stimulus for its production is the presence of acid in the duodenum The vagus nerves stimulate activity of the Brunners glands while the sympathetic nerves have an opposite effect

GASTRODUODENAL MOTOR ACTIVITY

Motor activity can be observed both when the stomach is empty and when it is full The movements of the empty

stomach give rise to the sensation termed hunger pangs The e hunger pangs are peristaltic waves which start in the upper stomach region and pass down to the duodenum

The motor activities of the stomach during digestion can be divided into two types gastric peristalsis and changes in muscle tone Gastric peristalsis consists of regular periodic contractions that segment off the distal end of the stomach and carry the portion of the gastric contents through the pyloric sphincter and into the small bowel In addition to these gross movements smaller changes — called "tone" changes — have been observed within the stomach These consist of a gradual shortening of the muscle fibers of the stomach as the volume of gastric contents decreases

The functions of the stomach during digestion include the reception of the meal mixing of the contents of the stomach and assuring passage of the gastric chyme into the small bowel This is a highly co ordinated function which has been carefully studied by Quigley and his co workers [5] He has observed that the distal portion of the stomach the pylorus and the first portion of the duodenum behave as a co ordinated segment and he has termed this the "antral pump It is his opinion that the pyloric sphincter s chief function is to prevent regurgitation of duodenal contents into the stomach

Several mechanisms operate to prevent any great increase in intragastric pressure when food enters the stomach Initially there is a relaxation of the walls of the stomach and a concomitant inhibition of motor activity The major portion of the food is held in the reservoir or upper portion of the stomach and at periodic intervals portions of the

mass are moved down into the antral pump segment The major stimulus for evacuation of the stomach is the size of the meal Therefore a large meal leaves the stomach more rapidly than a small one and for this reason frequent small feedings are advised for patients who have peptic ulcer The rate of gastric emptying is also regulated by factors acting within the duodenum It can be observed fluoroscopically that in some patients an initial bolus is passed into the duodenum and then there is no further gastric emptying An inhibitory reaction takes place within the stomach suppressing peristaltic activity The exact nature of this duodenal inhibitory regulation is not understood In other patients once emptying is initiated it is continued until the stomach is emptied of its contents

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ERODING FACTORS

CHEMICAL

The common denominator of all peptic ulcers is that they occur in tissues bathed by the acid gastric juice It is thou ht therefore that chemical factors play a large role in their genesis Experimentally ulcers can be produced by excessive acid secretion either by constant infusion of acid into the stomach or by constant stimulation of gastric secretion such as that with the use of histamine in beeswax High concentrations of acid must be present over a long period of time before ulceration occurs

Excessive acid secretion is probably present in the majority of ulcer patients This does not necessarily mean that this excessive secretion causes the ulcer It has been observed by Levin *et al* that the secretory rates of duodenal ulcer patients are considerably higher than the average secretory rate in patients without duodenal ulcers On the other hand patients with gastric ulcers have secretory rates which are lower than those of normal individuals It has been observed furthermore that the secretory rates of patients with duodenal ulcers are relatively constant and have little relationship to whether they are in a period of remission or a period of exacerbation It appears probable that some other factor produces the high ecretory rates seen in duodenal ulcers rather than that the ulcer itself directly produces the hypersecretion Some evidence has been shed upon this by the observation that vagotomy will abolish these high secretory rates This does not prove that the vagal overactivity is the sole cause of hypersecretion

The truism "no acid no ulcer first reported by Schwartz

3

ETIOLOGY

Benign ulcers of the esophagus stomach and duodenum have been termed peptic ulcers because they are found in the regions bathed by the acid gastric juice and because it is thought that the ulcer results in part from the eroding action of the gastric juice Peptic ulcer is not a single disease and cannot be ascribed to a single cause The ulcer is a local manifestation of a generalized disturbance which results in a circumscribed loss of the lining mucosa

During recent years a great deal has been learned about the causation of peptic ulcers Three factors have been implicated The first two involved in the production of all peptic ulcers are (1) the eroding factors which include both chemical and mechanical components and (2) local tissue resistance and defense factors The third factor as classified by Smith and Rivers is the systemic and constitutional diathesis factor that may be involved and that may determine to some degree which individuals will develop an ulcer Our present viewpoint is that peptic ulcer is the result of interplay of several or all of these factors differing in different persons and also changing in the same person under varying conditions

LOCAL TISSUE RESISTANCE AND DEFENSE FACTORS

There is no adequate explanation as yet for the localized nature of peptic ulcer If general factors operate why then does not the entire lining of the stomach digest away rather than just a localized area? It is thought by some that local tissue damage may occur predisposing to ulceration in that particular area This is a difficult problem to study It has been shown that with one type of experimental ulcer at least — the cinchophen ulcer — mucous secretion of the pyloric and duodenal glands is depressed It is possible that a decrease in mucous secretion may predispose to ulceration in this area

Hollander[5] has formulated the concept of the two component mucous barrier The first line of defense is the nonviable mucus which coats the inner lining of the stomach It is slowly removed by coagulation which is the result of its reaction with hydrochloric acid This serves to reduce the gastric acidity from 160 milliequivalents per liter to values below 75 milliequivalents per liter The mucus is regenerated by the underlying mucus producing cells Hollander has suggested that multiple deficiencies may impair the formation of mucus If loss of surface mucus continues the mucosa will suffer progressive denudation until the gastric tubules are exposed and a chronic ulcer may result

Attempts to supply exogenous mucus have been disappointing The commercial preparations available are variable and only weakly neutralizing When amounts are taken which are large enough to produce signifi

in 1910 remains valid Although there have been reports of ulcers in the presence of apparent achlorhydria the overwhelming weight of evidence indicates that free hydrochloric acid is necessary for the development of an ulcer As a general rule it can be said that peptic ulcer probably does not occur in the total absence of acid secretion

The presence of pepsin the digestive enzyme is also important in the development of ulcer and without pepsin ulceration probably does not occur Its role is less important than that of acid as it has been shown that pepsin has little effect in producing peptic ulcers in the absence of a high acid secretion Pepsin is necessary together with hydrochloric acid to produce ulceration but it is probable that acid has the predominant position

It may be that one of the problems presented by the ulcer patient is an inadequate neutralization of his own acid secretions Normally the surface or mucous cells of the stomach secrete an alkaline mucus which tends to neutralize the acid produced by the parietal cells and to protect the underlying mucosa [3] While there is some suggestion that this secretion may not be adequate in ulcer patients there are few definitive studies on this subject

Mechanical

Mechanical factors have an important role in the development of peptic ulcers [4] It appears that they have a relation to the location of the ulcer both in experimental animals and in human ulcer patients Ulcers tend to occur where there is the maximum degree of trauma to the stomach along the lesser curvature and also where the acid gastric contents are ejected from the stomach into the duodenum

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cant neutralization large gummy masses result in the stomach

There are other defense mechanisms possessed by the gastroduodenal tissues The cells themselves by their living nature have a certain resistance to digestion The neutralizing effect of the alkaline blood in the mucosal capillaries constitutes another defense mechanism There is a high concentration of the enzyme urease in the surface cells of the stomach Urease catalyzes the breakdown of urea to form ammonia and carbamate both of which aid in neutralizing the parietal secretion [6]

There are differences in the resistance of the mucous membrane in various parts of the stomach and in its ability to withstand the eroding action of acid gastric juice The fundus of the stomach is most resistant and the lesser curvature next to the pylorus is next most resistant The pylorus itself the duodenum the jejunum and the ileum show progressively decreasing resistance to acid erosion

Ischemia may be responsible for the local depression in mucosal resistance Certainly such factors may be important in preparing the soil so that a chronic ulcer can be implanted Poor vascularization of the first portion of the duodenum and the pyloric portion of the lesser curvature have been observed Palmer and Buchanan [7] have reviewed the problem of ischemia in relation to the genesis of ulcer They postulate the possible existence of an arteriovenous shunt mechanism which may be under either hormonal or neural control They further suggest that such a mechanism may be merely one of the stigmata of the ulcer patient

SYSTEMIC AND CONSTITUTIONAL FACTORS

The local eroding factors and the local defense factors of the stomach have been studied in detail and are well under stood The reason why the stomach is involved in an ulcera tive process in some individuals and not in others is less well understood It is probable that hereditary and consti tutional factors are important in leading to the development of a localized ulcer

Heredity

There are a number of studies which show that heredity may be concerned in human peptic ulcer These consist of surveys showing that the incidence of ulcer in certain fami lies is higher than in families of patients with other diseases We have had opportunity to follow one such family in which both parents and six children had peptic ulcers mainly of the severe variety which ultimately required surgery It should be pointed out that family suscepti bility is not equivalent to making a diagnosis of heredi tary illness Emotional economic and other environmental factors present in the family situation must be taken into consideration Studies have also been carried out on the incidence of ulcer in twins but the data are not entirely conclusive Our present knowledge indicates that hered ity is probably a predisposing factor as indicated by Draper and Tou aine in terming it a case of "selective environmental action upon a favorable constitutional ter rain"

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terogastrone has not been demonstrated to be effective in man after either oral or intramuscular administration

There is no evidence indicating an increased frequency of peptic ulcer in patients with primary endocrine disorders Indeed there appears to be a decreased incidence of peptic ulcers in both hypothyroidism and hyperthyroidism Peptic ulcer is also rare in hypoparathyroidism and hyperfunction of the parathyroid There is no striking relationship between chronic peptic ulcer and primary disease of the adrenal gland The occurrence of peptic ulcer during prolonged administration of corticotropin or cortisone has stimulated interest in the possible role of adrenal hyperfunction in the etiology and pathogenesis of peptic ulcer It has been observed that ACTH markedly increases uropepsin production and also stimulates the production of hydrochloric acid [10] (Fig 5) These effects may be observed after complete gastric vagotomy The frequency of occurrence of this stimulatory effect of corticotropin and cortisone is not known

The observations of the stimulatory effect of ACTH have suggested the concept that stress whether of emotional or physical origin may induce the hypothalamus to secrete a hormonal agent which stimulates the pituitary secretion of ACTH This corticotropin would then act to stimulate the adrenal glands to release cortisone and other steroids stimulating the gastric glands to secrete more acid and pepsin (Fig 6) Considerable attention has been paid to the physiologic mechanisms through which stress apparently produces its harmful effects Porter *et al* have measured the changes in the pH of gastric secretion after electrical

Hormones

The relationship of the hormones to peptic ulcer has been studied for many years This subject has recently been reviewed in detail by Kirsner [9] who points out that there is no consistent relationship between primary endocrine disturbances and chronic peptic ulcer in man Nonetheless there are certain endocrine relationships in peptic ulcer which should be noted Experimental observations on animals indicate that the gastrointestinal tract is highly sensitive to stressful conditions Ulcerations and erosions may follow stress Although ACTH has been implicated as a cause of erosions and ulcers such ulcerations can occur in the absense of the pituitary or adrenal glands

Local hormonal factors have also been implicated in the causation of ulcer The gastrointestinal hormones gastrin and enterogastrone have been identified As yet there is no conclusive evidence that gastrin produced by antral hyper function has any important role in the development of peptic ulcer in patients

Enterogastrone inhibits gastric secretion in dogs when administered intravenously but is not effective by other routes of administration Enterogastrone and related substances such as urogastrone and anthelone have been shown to inhibit gastric secretion in experimental animals They are also capable of delaying or preventing the appearance of ulcers in Mann Williamson dogs even when given in doses too small to depress secretion of hydrochloric acid The mechanism of their action is not known The favorable results in dogs were obtained after intravenous injection En

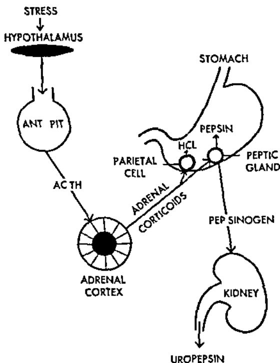


FIGURE 6

Hormonal pathway by which stress may induce increased gastric acid and pepsin (From Gray *et al* [6] Reproduced with kind permission of the editor of *Gastroenterology*)

is by action on the anterior hypothalamic nuclei which is transmitted to the stomach by way of the vagus nerve The second mechanism is the result of stress acting on the posterior hypothalamic nuclei which in turn stimulates the posterior pituitary causing an increase in the output of adrenalin by the adrenal gland The adrenalin in turn stimulates the anterior pituitary to produce ACTH which

stimulation of the nuclei of the anterior hypothalamus and also after stimulation of the posterior hypothalamus When the anterior hypothalamus was stimulated there was a rise

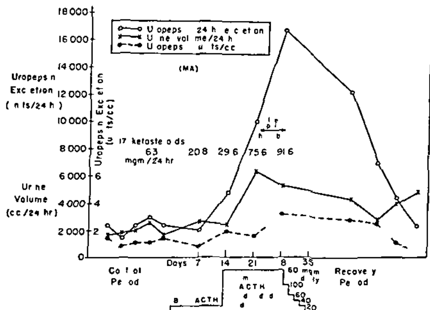


FIGURE 5

Uropepsin response to ACTH after vagus section (From Gray *et al* Reproduced with kind permission of the editor of *Gastroenterology*)

in gastric acidity which could be completely abolished by a bilateral vagotomy Stimulation of the posterior nuclei also produced an increase in gastric acidity which could be eliminated by adrenalectomy Utilizing this data Shay has suggested that there may be two mechanisms whereby stress acts to stimulate gastric secretion The first of these

erosion may occur secondary to autonomic discharge Curling's ulcer which follows severe burns is an example[1]

The association between emotional trauma and subsequent hemorrhage or perforation is well known Ulcer perforation increased during the period of heavy air raids over Britain during World War II[18] These observations are consistent with the theory of anxiety as a causative factor in ulcer

Wolf and Wolff[19] have studied the relation of emotional states to the gastric mucosa in their fistulous subject Tom Two types of reactions were noted A depression of acid output motor activity and vascularity was associated with withdrawal from stressful stimuli An enhancement of acid output motor activity and vascularity was associated with repressed or unexpressed aggression It was also observed that it was possible to abolish the "stress" reactions of the stomach with vagotomy

While it is tempting to try to apply these observations to the general theory of the etiology of peptic ulcer it is hazardous to do so Individual variations exist and it is probable that not all stomachs react in the same way to the same stress Furthermore it is known that although stress affects the gastrointestinal tract in other conditions such as irritable colon organic changes do not result from chronic stress

Personality

Although it is evident that peptic ulcer is not limited to certain types of persons it has been observed that some personality factors are more closely associated with ulcer than with other disease conditions Most of the investigations

stimulates the production of cortisone and other corticoid substances by the adrenal gland Much more information concerning the status of the hypothalamic pituitary and adrenal axis in peptic ulcer will be necessary to determine the general applicability of this concept

The fact that peptic ulcer is much more common in men than women is well known but the reason for this sex difference has never been adequately explained It has been suggested that the greater exposure of men to environ mental influences and stress may predispose to the develop ment of ulcers The low incidence of ulcer in adult women during the active reproductive period and the apparent healing of ulcer early in pregnancy suggest a protective influence from the female sex hormones Further study must be done in order to clarify the mechanism whereby preg nancy exerts its beneficial effects

Neurogenic Factors

Hemorrhages erosions and acute ulcers of the stomach duodenum and small bowel can occur following intracra nial injury [3] Davis *et al* [1] recently reported 48 instances of acute ulceration or hematemesis which followed neuro surgical procedures in a series of 7000 patients Acute ulcers were demonstrated in most of these patients There are cer tain differences between these acute ulcers and chronic pep tic ulcer There is some evidence that such neurogenic ulcers may be related to the adaptation syndrome [16] The gas trointestinal tract reacts readily to stress Beaumont in his studies on Alexis St Martin noted that reddening of the mucosa might follow an emotional upset It has also been observed that acute gastric and duodenal hyperemia and

may be a problem relating to the patient's occupation something over which the patient has little or no control These findings have considerable importance in the treatment of the ulcer patient and will be discussed in more detail in Chapter 11

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have been uncontrolled and have depended upon subjective assessments for conclusions *Furthermore the investigations* that have been carried out have been with patients after they developed their ulcers It would be of interest to know whether any discernible changes were noted in their personalities after the establishment of the ulcer as compared with prior to the development of the ulcer Considerable clinical investigation remains to be done on the interrelation of certain aspects of the personality hypersecretion and other factors which bring about an ulcer

Sullivan and McKell [2] describe the ulcer patient as tense anxious and driving Typically he is a go getter promoter manager or executive Not infrequently it is observed that patients with ulcers hold down several jobs at the same time and are very productive people Ulcer patients tend to have the driving personality and ambition which make for success in the business world They are willing to shoulder responsibility and have a high degree of self reliance

Sexual adjustment is usually good in patients with ulcers They have the highest marriage rate and one of the lowest divorce rates among patients with gastrointestinal disorders

Sullivan and McKell also point out the craving for superiority *which seems to be such an important part of the* personality of the ulcer patient This craving may be practically insatiable during the most active decades of adult life

The ulcer personality may have some relation to the pattern of recurrences It has been noted that fatigue emotional conflict and infection are responsible factors in determining recurrences The emotional conflict frequently

4

PATHOGENESIS

The events which lead to the development of an ulcer are difficult to describe As we have said it is known that there are multiple factors in its development and that these factors are not necessarily the same in all individuals From the great frequency of the condition it is apparent that the balance between the eroding and the defense factors is a very delicate one and little is required to disturb this balance

DEVELOPMENT OF AN ULCER

The sequence of events which occurs during the development of an ulcer under usual circumstances is not known When the patient seeks medical advice the ulcer is usually already present If it is in a gastroscopically visible area the healing of the ulcer can be visualized Most ulcers however are in the duodenum and are not accessible to direct visualization Examination of stomachs removed at operation or at autopsy is of some help in tracing the development of ulcers It has been observed that acute subacute and chronic ulcers can be found The available evidence indicates that the chronic peptic ulcers of the stomach

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bowel ulceration of the jejunum results even more uniformly. The character of the diet has some relation to the development of these experimental ulcers. Ulcers develop more rapidly if the diet is coarse and harsh and their development is delayed if the diet is soft.[3]

There are similarities between the experimentally produced ulcers and chronic peptic ulcers in man. A decrease in the defense reactions of the mucosa to gastric hydrochloric acid appears to be the most common factor in the formation of experimental ulcers. This can be the result of diverting the alkaline duodenal contents so that gastric acidity is unbuffered. It can also be the result of alteration of the blood supply by administration of agents which increase vascularity, such as histamine or caffeine. Defense mechanisms can also be broken down by necrosis of the mucosal cells such as occurs in the cinchophen ulcer.

Structural Alterations

In the experimentally produced lesions either of two pathologic mechanisms appears to be present. Necrosis of the mucosal cells with or without hemorrhage may take place. The cinchophen ulcer is an example wherein the initiating factor is necrosis of the mucosal cells. Hemorrhage may be the primary change and may be followed by necrosis. This occurs in the lesions produced by histamine and by caffeine. The two processes of necrosis and hemorrhage may occur simultaneously.

Although it is hazardous to transpose results obtained in the experimental laboratory to human practice, the work on experimental production of ulcers has been extremely helpful in advancing our understanding of naturally occurring

or duodenum probably have their origin in an acute ulcer The initial process is doubtless the development of an erosion or ulcer which goes on to form a chronic peptic ulcer unless the balance is restored between the eroding and the defense mechanisms

While it is not possible to follow the development of ulcers from the acute to the chronic stage in human subjects it is possible to do so with the experimental ulcers that can be produced in animals Erosions and superficial ulcerations are frequently seen in animals but chronic peptic ulcer is rare Peptic ulcers can be produced however by a variety of methods Ligation of the distal portion of the stomach results in the formation of an ulcer fairly regularly Agents which stimulate gastric secretion and produce hyperemia can be used to produce experimental ulcers Histamine in beeswax and caffeine both will produce ulcers in experimental animals In both of these circumstances there is an increase in vascularity as well as an increase in the secretion of acid Cinchophen has also been employed to produce ulcers in experimental animals Its effect appears to be the result of a direct toxic action on the mucosal cells

The most commonly employed method is the performance of a short circuiting operation This operation the so called Mann Williamson procedure consists of anastomosing the mid portion of the small bowel to the stomach so that a gastrojejunostomy is performed After this operation ulceration of the jejunum results in approximately 10 to 25 per cent of the experimental animals This is due to the lower resistance of the jejunum to the acid gastric juices If the alkaline pancreatic juice and bile which normally protect the jejunum are diverted into the lower small

some role in the development of peptic ulcer. Mechanical factors appear to favor the production, maintenance, and aggravation of peptic ulcers.[1-4] It has been observed that duodenal ulcers occur most frequently in the area where the acid gastric chyme is ejected from the stomach into the duodenum. Alterations in motor function are a common observation in ulcer patients. This may be manifested by spasm at the site of an ulcer or in distant locations of the stomach or duodenum. These motor changes have been correlated with the symptoms of ulcer patients.[5, 6]

In their classic studies on their fistulous subject, Wolf and Wolff[7] observed that hypersecretion was accompanied by hypermotility and an increase in the blood supply to the *mucosa. These circumstances made the mucosa more sus*ceptible to trauma and also increased its sensitivity. It appears likely that these alterations in function are important in the pathogenesis of a peptic ulcer. What is not known, however, is whether these alterations are present prior to the development of the ulcer or whether they can be observed only after an ulcer has developed.

PATHOLOGY OF PEPTIC ULCER

In contrast to the pathogenesis of ulcer, the pathologic features of peptic ulcer have been well documented. It was the pathologist who first diagnosed and recognized peptic ulcer, while our clinical knowledge of the disease came at a later date.

A peptic ulcer has been defined as a benign nonspecific ulcer which penetrates the muscularis mucosae and is located in the portions of the alimentary tract which are

ulcers It seems probable that the basic pathologic changes are similar in the two situations These experimental agents have also been of inestimable value in the assessment of various therapeutic agents which have been proposed for the treatment of peptic ulcer

Functional Alterations

In addition to the structural alterations which have been discussed alterations in function can occur which may have some bearing on the development of peptic ulcer These for the most part consist in alterations which affect the balance between the eroding and the defense factors of the stomach

Considerable attention has been paid to the character of the gastric secretion The volume and acidity of gastric secretion is higher in patients with duodenal ulcers than in normal individuals [3] Secretory rates in patients with gastric ulcer are lower than those in normal individuals however and it does not appear that hypersecretion plays a significant role in the development of gastric ulcer The mere fact that a patient may have high acid levels does not explain why he should develop an ulcer Most authorities feel that one must postulate a breakdown in the defense mechanism in a local area There is some evidence that inadequate neutralization of the hydrochloric acid formed by the parietal cells may account for high acid values This could be the result of a deficient formation of alkaline mucus by the non parietal cells This mucus normally serves to protect the mucosa of the stomach from digestion In the presence of high acid values however the mucus tends to be precipitated and in time the mucosa may be denuded

It is likely that the motor functions of the stomach have

fective processes such as peritonitis or respiratory infections Erosions and acute ulcers of the stomach (Curling s ulcers) have also been observed to follow extensive burns



FIGURE 7

Photograph of an acute duodenal ul er which perforated (From Di is *et al* Repr d ced with kind permission of the ed tor of *Surgery Gynecolog and Obstetrics*)

of the skin Acute ulcers also follow other forms of stress and they have been observed to accompany injury or surgery of the br un

It is not known what relation these acute ulcers have to chronic peptic ulcer It is probable that the majority of

bathed by acid gastric juice It is distinguished from acute erosions which may occur in the absence of hydrochloric acid These erosions usually go on to heal without developing into chronic peptic ulcers Peptic ulcers may be divided into acute ulcers subacute ulcers and chronic ulcers Initially it was thought that all chronic ulcers originated as acute ulcers Subsequently there developed a school which believed that chronic peptic ulcer was a separate disease bearing little relation to acute ulcer More recently these two points of view have merged and although there is no incontestable evidence for it it is thought now that most chronic ulcers have their origin in an acute ulcer or in an erosion The subacute ulcer represents merely a transition phase between acute and chronic ulcer

Acute Ulcers

Acute ulcers are those ulcers of short duration which are frequently seen at autopsy but are relatively unimportant in clinical practice They can be distinguished pathologically from chronic ulcers[8 9] Stewart[11] has made an extensive study of acute ulcers and he has noted that acute and chronic ulcers of the stomach and duodenum not infrequently coexist In the stomach acute ulcers are frequently multiple but in the duodenum they are more likely to be single Multiple acute small ulcers are rather variable in size and in shape and although they tend to occur in regions where chronic gastric and duodenal ulcers predominate they may also occur anywhere in the stomach or duodenum An example of an acute duodenal ulcer which perforated is shown in Figure 7

The majority of acute ulcers are associated with acute in

Chronic Ulcers

Chronic ulcers account for the majority of symptoms in ulcer patients These chronic ulcers are located in the distal esophagus and in specific parts of the stomach and duodenum Most esophageal ulcers are associated with other conditions but they do occur rarely as a primary entity They have accounted for 4 per cent of peptic ulcer at autopsy [13] The most common associated condition is hiatus hernia Some so called esophageal ulcers actually represent ulceration of the herniated gastric segment [1]

When involving the stomach they occur with greatest frequency on the lesser curvature side of the stomach 85 per cent of gastric ulcers being in this region They are more commonly located in the distal stomach, approximately 60 per cent of gastric ulcers being within 6 cm proximal to the pyloroduodenal junction The pyloric channel is the site for 12 per cent of gastric ulcers [1] and 4 3 per cent of all peptic ulcers Benign ulcers of the greater curvature of the stomach and of the fundus are rare

The location of duodenal ulcers is also sharply demarcated with 95 per cent of duodenal ulcers being within the first 3 cm of the duodenum Rarely duodenal ulcer is seen to involve the second or third portions of the duodenum Ulcers in this location are referred to as postbulbar ulcers The anterior and posterior walls of the duodenum are involved with about equal frequency Sometimes kissing ulcers" may be present involving both the anterior and posterior walls of the duodenum at the same time Duodenal ulcers involving the posterior wall are the most difficult to demonstrate radiologically and at operation They are also

acute ulcers heal without ever going on to form chronic peptic ulcer Certainly there is no clear cut evidence that nonexperimental chronic ulcer originates from an erosion or an acute ulcer but on the other hand there is no evidence to dispute this point of view

It has been shown conclusively that experimentally produced acute ulcers can ultimately become chronic ulcers The differences between acute and chronic ulcers appear to be quantitative rather than qualitative If the defense forces are adequate the acute ulcer will probably heal whereas if the defense forces are inadequate and the eroding forces are not held in check a chronic ulcer may develop

These acute ulcers have little clinical importance They are responsible for some of the cases of gastrointestinal bleeding for which no source can be found Even though careful x ray studies are carried out during the bleeding or shortly thereafter no abnormalities can be observed The acute ulcer crater is so superficial that one cannot demonstrate a niche and secondary signs of ulceration are usually absent also Acute ulcers can also perforate frequently without any prior warning Their most important feature appears to be in relation to therapy for peptic ulcer Care must be taken in evaluating any therapeutic technique to distinguish those patients who have acute ulcers from those who have chronic or recurrent ulcers Acute ulcers tend to heal spontaneously without any rigorous sort of treatment and are not prone to recur Their response to treatment therefore is quite different from that of chronic ulcer and they could give to a misleading impression of the value of the therapy under study

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most likely to bleed and to form perforated walled off ulcers Ulcers involving the anterior wall are less prone to bleed but more prone to perforate

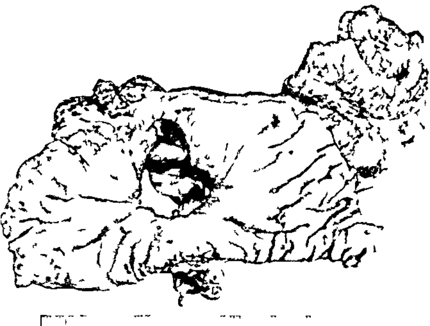


FIGURE 8

Photograph of a gross specimen showing a chronic gastric ulcer which had perforated into the pancreas

Gastric ulcers are almost always solitary but multiple gastric ulcers are seen on occasion Duodenal ulcers tend also to be single but two or three ulcers may be found at times Gastric and duodenal ulcers commonly are present together This is said to occur in 15 per cent of patients with gastric ulcers

Gastric ulcers are usually about 1 cm in diameter but

ulcers three or four times this size are not uncommon Their gross appearance is rather striking Chronic gastric ulcers usually have a deep crater with sharp marginal edges and a clean base The base of the ulcer is whitish gray and consists of a thickened subserosal coat The outline of the edge of the ulcer is usually regular (Fig 8)

Duodenal ulcers are relatively small and as such are not easily recognized grossly A small white puckered scar on the subserosal coat may provide the only external evidence of the disease If the ulcer is located down the posterior wall of the duodenum it is almost impossible to diagnose it merely by palpation A duodenostomy has to be performed under these circumstances to rule in or out the presence of an ulcer located on the posterior wall

The microscopic features of ulcers are similar There is a loss of the mucosa down to the muscularis mucosae The lining of the crater has four zones (1) purulent exudate (2) a thin coat of fibrinoid necrosis (3) granulation tissue and (4) an outer dense layer of scar tissue These layers cannot always be clearly defined and the appearance of the lesion varies considerably depending both on its activity and on its duration Blood vessels in the base of the ulcer are numerous in the acute form but in chronic ulcer they may be obliterated by endarteritis as a result of the ulceration and scarring (Fig 9)

HEALING OF ULCERS

Acute ulcers heal rapidly without any evidence of residual scar Many chronic ulcers also heal completely but at autopsy or operation a scar of the previous ulcer can be



FIGURE 9
Photomicrograph of a chronic gastric ulcer

recognized It is of interest that at autopsy the incidence of healed ulcers is equal to that of active ulcers [17] The healed duodenal and gastric ulcers indicate the presence of peptic ulcer sometime earlier This is not surprising as peptic ulcer is not a static process but the end result of periodic erosion and healing

During the erosion development phase of the ulcer the ulcer deepens and the mucosa may be undermined Scar tissue is formed in the base of the ulcer and endarteritis may diminish the blood supply to the base of the ulcer These all present obstacles to healing of the chronic ulcer The layer of necrotic material which so frequently forms the base of the ulcer provides no footing for ingrown epithelium and a dense scar may prevent approximation of the edges of the ulcer The most potent factor in the retardation of healing is the factor which originally produced the ulcer – the erosive action of acid gastric juice Merely diverting the acid gastric juice as is done in gastroenterostomy may be sufficient to produce prompt healing of the ulcer

When an ulcer is seen in the healing phase the signs of inflammation about the ulcer disappear and the ulcer is reduced in size This reduction is produced by a shrinkage of the base of the ulcer and filling in of the crater by granulation tissue from below and from the sides The shrinkage of the base results in some puckering of the overlying serosa The shrinkage also can be observed to distort the rugae of the stomach with the result that the folds radiate into the site of the previously active ulcer A similar process may take place in the duodenum This accounts in part for the distortion of the duodenal cap in patients with chronic or recurrent peptic ulcer If sufficient scarring of the stomach



FIGURE 9
Photomicrograph of a chronic gastric ulcer

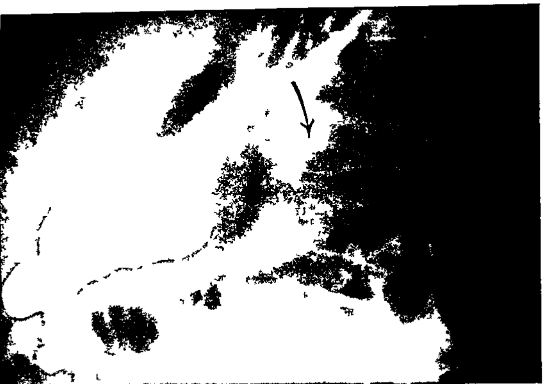


FIGURE 10

X-ray showing a gastric ulcer in its location with hourglass deformity of the mid stomach

or duodenum occurs actual organic changes may take place in its contour Stenosis of the pyloric area may develop so that there is gastric retention Ulcers in the mid portion of the stomach may cause sufficient scarring to produce the hourglass type of deformity Here the stomach consists of two chambers an upper and a lower which are connected by a narrow passage as illustrated in the following case

F D a 62 year old woman had a perforated ulcer in 1925 which was closed A large gastric ulcer developed in 1950 healed and recurred in December 1952 This gastric ulcer again recurred in September 1953 X ray (Fig 10) showed a gastric crater directed posteriorly with severe hourglass deformity of the mid stomach this was confirmed by gastroscopy The patient developed a second ulcer located in the antrum which was resected Both lesions were benign

Healing and scarring in the duodenal bulb area produces a deformity of the bulb which at x ray resembles diverticulum Scarring of the postbulbar area may very rarely produce jaundice due to changes in the area of the ampulla of Vater

The amount of time necessary for complete healing to take place has been studied in ulcer patients Few of these studies have been well controlled and even the range of values of the better studies is rather wide It has been reported that chronic gastric and duodenal ulcers will heal in from 14 to 100 days the average being 40 days[1] This assumes that the patient is under strict medical management It has been claimed that various therapeutic approaches including resin therapy and the cholinergic blocking agents significantly shorten the healing time There appears to be no valid statistical evidence to support this contention and it is doubtful whether such evidence could be obtained[1] It is

16 RUFFIN J M JOHNSTON D H CARTER D D and BAYLIN G J The clinical picture of pyloric channel ulcer *J A M A* (in press)
17 MOORE R A *Textbook of Pathology* Philadelphia Saunders 1944
18 IVY A C GROSSMAN M I and BACHRACH W H *Peptic Ulcer* Philadelphia Blakiston 1950 p 161
19 RUFFIN J M TEXTER E C JR CARTER D D and BAYLIN G J *J A M A* 153 1159 1953

known that the healing time is dependent upon the size of the ulcer the duration of the lesion and the amount of scarring present and on other factors including whether the ulcer is actually a chronic ulcer or merely an acute ulcer which has been classified as a chronic one

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but on occasion it may become so severe as to require narcotics for relief

Location and Radiation

Ulcer pain in uncomplicated gastric and duodenal ulcer is located in the upper abdomen near the midline somewhere between the xiphoid cartilage and the umbilicus. The pain is circumscribed in a relatively small area and the patient can often indicate the location of the pain by covering this area with one finger. Pain arising from duodenal ulcer characteristically is more confined than pain from gastric ulcer. In fact one may see very bizarre types of pain in patients with gastric ulcer.

Radiation of the pain is not common in uncomplicated ulcer. If complications occur the symptomatology becomes changed. The most common complication accounting for this is the development of a perforated or walled off ulcer. Under these circumstances one may have radiation of the pain to the back or to other parts of the abdomen. The symptomatology of the complicated ulcer is discussed in more detail in Chapter 12.

Rhythm

A very characteristic feature of the peptic ulcer syndrome is the rhythmic appearance and disappearance of pain in relation to the state of fullness or emptiness of the stomach. The pain usually has a definite relation to the ingestion of food coming on gradually for a period of half an hour or an hour and if it is not relieved by medication it may pass off spontaneously. The interval between ingestion of food and onset of the pain may vary from a half hour to more than 3

5

SYMPTOMATOLOGY

Pain is the outstanding symptom of peptic ulcer. This pain is so characteristic that it frequently suffices to indicate the diagnosis almost without further examination. Paradoxically, however, the character of the pain is difficult to describe. Some would even object to calling it "pain," preferring to call it distress. It is probable that there is not just one type of ulcer pain but that there are several types having different characteristics and perhaps different mechanisms.

CHARACTERISTICS OF ULCER PAIN

Four characteristics have been described in relation to ulcer pain. They are as follows: (1) the nature and intensity of the pain, (2) location and radiation of the pain, (3) the rhythm of the pain, and (4) the periodicity of the pain.

Nature and Intensity

Ulcer pain is most often described as a gnawing, aching or burning sensation. It may resemble hunger contractions and some patients find it difficult to differentiate from hunger sensation. The degree of pain may vary markedly from patient to patient. Usually it is dull and not incapacitating,

but on occasion it may become so severe as to require narcotics for relief

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hours It is said that the interval is shorter in gastric than in duodenal ulcers Some patients will deny that the pain has any relation to their food intake They are however usually able to indicate that they feel better when their stomach is full than when it is empty

In more severe cases nocturnal pain occurs This comes from 1 to 4 hours after retiring The patient is awakened from sleep by the pain which may continue for an hour or more Ulcer pain is characteristically absent in the morning on arising and usually does not make its appearance until *after the first meal*

If complications develop such as walled off perforation or obstruction the symptoms are altered so that the usual rhythmicity of the ulcer pain is no longer present

It is helpful in the diagnosis of ulcer pain to ascertain what methods the patient uses to obtain relief As indicated above the patient usually notes that ingestion of food or milk or antacids will relieve the pain within a brief period Absorbable alkalies such as baking soda usually afford more prompt relief than that noted with the nonabsorbable antacids Patients with gastric ulcer can sometimes obtain relief of their pain by belching Temporary relief may occur from the ingestion of almost any type of liquid Sometimes patients with gastric ulcer will indicate that the ingestion of warm or hot liquids gives relief External heat also may relieve ulcer pain

Periodicity

One of the most striking diagnostic features of peptic ulcer pain is its periodicity The pain tends to be present for days or weeks at a time and then the patient may be asymp

tomatic for long intervals Recurrences are most likely to occur during the spring and fall months (Fig 11) Recurrences have also been observed to have a relationship to anxiety and tension respiratory infections and dietary indiscretions

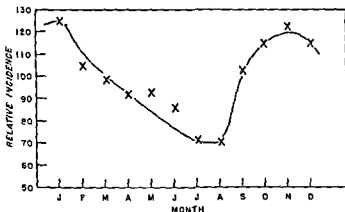


FIGURE 11
Seasonal incidence of ulcer in the Northern Hemisphere

PAIN AS AN INDEX OF ULCER ACTIVITY

Pain constitutes the main symptom in peptic ulcer and is the one most frequently used to estimate the activity of the ulcer As we have indicated the pain characteristically will come on for days to weeks at a time and then be absent for equally long or longer intervals During these periods of remission it is frequently assumed that the ulcer has healed This is not necessarily the case since an x ray or gastroscopic examination sometimes reveals that the ulcer is still

present A partial explanation of this phenomenon is that during these quiescent spells the ulcer tends to heal raising the pain threshold

CAUSE OF ULCER PAIN

The fact that ulcer pain occurs after meals at a time when gastric acidity may reach its maximum level has given rise to the theory that acid causes the pain This theory was advanced by Bonninger in 1908 He reported that the introduction of 0 1 normal hydrochloric acid into the stomachs of patients with gastric ulcer invariably produced pain and suggested its use as a diagnostic test

Motor disturbances have also been proposed as the cause for ulcer pain Lennander[3] observed that the stimuli for production of pain from the gut arose from tension or compression of the mesentery and he concluded that ulcer pain like other forms of visceral pain arose from motor disturbances such as spasm His theory received support from Hurst[4] who thought that achalasia of the pyloric sphincter in the face of an advancing peristaltic wave caused the pain Carlson carried out studies on intragastric pressure and concluded that ulcer pain was synchronous with waves of increased intragastric pressure A general increase in gastric tone and contraction of the duodenal cap have both been implicated as causing the pain

Dragstedt and Palmer showed that rubbing the serosa over an ulcer also produced typical pain in a patient who had been explored under local anesthesia They noted that pain could result from compression of the ulcer or contraction of the duodenum and when pain occurred it was ac

companied by deep circular contraction rings just distal to the ulcer and was succeeded by similar spasms with severe cramplike pain Quigley[9] has made extensive studies of the motor physiology of the stomach He has observed that the antrum pyloric sphincter and duodenum work in a co ordinated fashion He has concluded that the continuous burning pain arises either from "a spasm in the region of the ulcer from swelling and inflammation around the border of the ulcer or from contact of the ulcer with gastric acid Since hydrochloric acid–pepsin mixture exerts an anesthetic action on human skin and does not produce pain in the normal stomach it is suggested that in the patient with ulcer gastric acid must act indirectly and produce pain by inducing abnormal motility in the region of the ulcer [9]

Despite the fact that physiologists hold that the stimuli for visceral pain are those of tension or compression of the mesentery the most commonly held theory of ulcer pain is that it is due to direct chemical irritation by the hydrochloric acid The strongest support for the acid concept of ulcer pain comes from the observations of Palmer [1] who revived the acid test of Bonninger as a diagnostic test for peptic ulcer He reported that following instillation of 200 cc of 0 1 normal hydrochloric acid into the stomach in patients who were in the active phase of ulcer ulcer pain would develop in 95 per cent of cases Concomitant x ray and fluoroscopic studies were not carried out Bonney and Pickering extended these observations and reported that pain developed in 86 per cent of their patients following ingestion of acid They studied the x ray appearance of the stomach at the same time and could not correlate pain with

any of the x ray characteristics Palmer and Pickering concluded independently that pain was not usually dependent upon gastric or duodenal tone or motility or the presence of pylorospasm Palmer stated that "the pain induced by the acid is in all probability due to direct irritation of the nerve ending by the acid solution [13] Palmer's and Pickering's work is supported by that of Rowlands and Friedlander [14] who recorded gastric and duodenal motility with intragastric balloons They could find no evidence of either spontaneous or acid induced pain as related to muscular contractions or increase in tone

Several criticisms can be made of the theory of direct chemical irritation of the nerve fibers by hydrochloric acid [15] We have been unable to confirm Palmer's and Pickering's findings [16] One hundred "acid tests" were performed on 88 patients with active ulcers Only 37 per cent of patients developed or continued to have ulcer pain after introduction of acid In 45 cases no pain was produced following administration of acid and in 18 patients having spontaneous pain the introduction of acid was followed by complete relief within a few minutes There was no correlation between the height of acidity and the development of pain When "acid barium was used to study the relationship between motility and the development of pain it was observed that the alterations in motility were associated with the pain This is illustrated by the following case

D G a 39 year old man had experienced intermittent ulcer distress for 15 years Following administration of 200 cc of 0 5 per cent hydrochloric acid by Levin tube he developed severe epigastric pain This was followed by 200 cc of acid barium without change in pain pattern Gastric peristalsis was active but there was only minimal emptying

The pain was completely relieved by 50 mg of Banthine given intramuscularly Gastric acidity was unchanged after gastric intestinal motility ceased coincident with administration of the anticholinergic drug (Fig 12)

Bloomfield in reviewing the criticisms of this "acid theory" also points out that pain is rarely noted before break

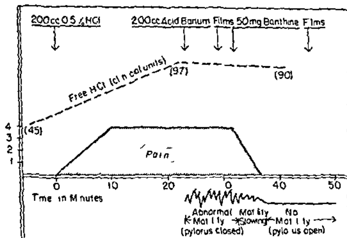


FIGURE 12

Relation between acidity, motility and pain following introduction of 0.1 normal hydrochloric acid in the stomach of an ulcer patient (From Ruffin *et al* Reproduced with kind permission of the editor of *Gastroenterology*)

fast even though the acid level is high at this time The acid theory likewise does not account for the intervals of remission with ulcer pain absent for long periods of time It is difficult to explain the pain of gastric ulcer by the acid theory because patients with gastric ulcer usually have acidities which are lower than normal The acid theory also does

not explain the relief of pain which occurs even though the acidity of the stomach is unaffected It is a common clinical observation that relief of ulcer pain occurs promptly on admission to the hospital where the only treatment prescribed is rest sedatives and diet therapy which does not greatly alter the gastric acidity

There are at least four possible explanations for the relief of ulcer pain (1) diminution or absence of free hydrochloric acid at the ulcer site (2) alteration of motor activity (3) interruption of the sensory pathway and (4) elevation of the pain threshold[17] Hydrogen ions can be removed by vomiting aspiration of gastric contents or neutralization Subtotal gastric resection acts by removal of the mechanism for hydrochloric acid production Motor activity can be altered by chemical blockage of cholinergic impulses at the ganglionic level and the effector site or surgical section of the vagus nerve Pain can be relieved by interruption of the visceral afferent pathway Ulcer pain can also be relieved by elevation of the pain threshold This is shown schematically in Figure 13

Studies of gastrointestinal pain have been carried out by Wolff and Wolf They have observed that noxious stimuli for gastrointestinal pain are (1) engorged or inflamed mucosa (2) extension or spasm of the muscular elements of the bowel and (3) traction upon the mesenteric attachments In their studies of the fistulous subject Tom they noted that the mucosa of the stomach was insensitive to pain produced by the blades of forceps or application of local chemical irritants when the mucosa was normal When the mucosa became inflamed however local mechanical and chemical stimuli evoked pain Contractions of the stomach

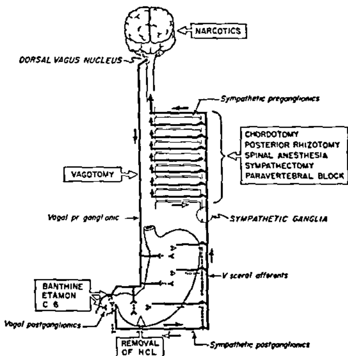


FIGURE 13

Schematic representation of the mechanisms of relief of pain in peptic ulcer (From Legerton *et al* [7] Reproduced with kind permission of the editor of the *Southern Medical Journal*)

against an indwelling balloon induced pain and when the mucosa became engorged pain was produced at a lower pressure level They felt that this pain arose from deeper layers of the stomach either the muscularis mucosae or the serosa

Illingworth has attempted to reconcile the several conflicting points of view He describes three types of ulcer

pain diffuse pain localized pain and tension pain Diffuse pain comes closest to being typical ulcer pain Localized pain has some of the characteristics of somatic pain it is most likely to occur when the disease involves the pylorus and the symptoms are relieved by vomiting

There is no question that the acidity of the gastric contents is essential to the production of pain The question remaining is whether the pain is mediated directly by chemical irritation or indirectly by such an agent as reflex hyperemia disordered motility or both Illingworth feels that hyperemia which may be in part secondary to raised acidity may explain both diffuse and localized pain This would also provide the reason why the patient is so frequently free of pain in the morning and why pain is absent following hemorrhage The third type of pain tension pain reconciles the observations of Hurst of Carlson and of Ruffin who have noted that ulcer pain can be correlated with abnormal motility and can be relieved by some procedure which interrupts the abnormal motility A concept of the production of ulcer pain using the latter ideas is presented in Figure 14

OTHER SYMPTOMS OF PEPTIC ULCER

Nausea and Vomiting

Neither nausea nor vomiting is a frequent symptom of uncomplicated peptic ulcer When they occur nausea and vomiting are more likely to be symptomatic either of gastric retention or of an irritative ulcer near the pylorus Irritative vomiting occurs soon after the meal and the patient notices relief of his ulcer distress following the vomiting On

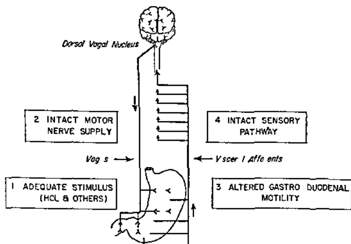


FIGURE 14

Schematic representation of one concept of the mechanism of production of ulcer pain (From Ruffin *et al* Reproduced with kind permission of the editor of *Gastroenterology*)

the other hand obstructive vomiting is likely to come on in the early hours of the morning and food eaten in the previous meal can be observed in the vomited material

ERUCTATION AND WATER BRASH

Eructation and water brash can occur in peptic ulcer but both are rare symptoms Eructation sometimes produces relief of distress in patients with gastric ulcer

CONSTIPATION

Constipation is a frequent complaint among ulcer patients It is probable that constipation is not directly related to the ulcer and it is not infrequently the result of the re

strictive ulcer type of diet along with a constipating type of medication Constipation is also frequent in patients who have pyloric obstruction

Hematemesis and Melena

Hemorrhage may be the initial symptom of peptic ulcer The incidence of hemorrhage as the first symptom of ulcer varies from 3 to 50 per cent with an average of 16 2 per cent *Bleeding* as an initial symptom is more common in gastric than in duodenal ulcer

SYMPTOMATOLOGY AS RELATED TO LOCATION OF ULCER

Esophageal Ulcer

The usual symptoms of esophageal ulcer are pain and dysphagia The pain of esophageal ulcer is located in the substernal region It is frequently accompanied by heart burn and substernal distress Its relation to food intake is less characteristic than the pain of gastric and duodenal ulcer The pain has two relationships to food ingestion the first being the pain which occurs on swallowing This is as*sociated with the passage of the food over the ulcer Thus* coarse foods are more likely to cause ulcer pain than soft bland foods In addition the patient with an esophageal ulcer may have pain 30 minutes to 2 hours after the food has been ingested which may be in part due to reflux of acid gastric contents into the esophagus

Dysphagia is also common in patients with esophageal ulcer This is most likely to occur on swallowing solids and is related to the inflammation and spasm in the region of

the ulcer The hiatus hernia which is present in most patients with esophageal ulcer contributes to the dysphagia

Gastric Ulcer

In general the symptoms of gastric and duodenal ulcers are similar although it should be emphasized that the rhythm and symptoms of gastric ulcer pain are much less characteristic of duodenal ulcer If a gastric ulcer is located high in the stomach it may be asymptomatic

Moynihan attempted to distinguish between gastric and duodenal ulcers by symptomatology Whereas the duodenal ulcer cycle is given as food comfort pain Moynihan felt that gastric ulcer has a cycle of food comfort pain comfort This sequence of events is as follows food is taken and for a brief period comfort is experienced lasting perhaps half an hour to an hour and a half This is followed by an episode of pain which may disappear when the stomach no longer contains food Actually the symptoms of gastric ulcer more frequently resemble duodenal ulcer than those of gastric ulcer as described by Moynihan This is in part due to the fact that duodenal ulcers and gastric ulcers are not uncommonly associated with one another in the same patient duodenal ulcer being present in 15 per cent of patients with gastric ulcers Likewise because the antral pyloric and duodenal segments behave as a unit ulcers in this area of the stomach tend to stimulate the symptoms of duodenal ulcer

When the gastric ulcer is flat or shallow pain is poorly localized If the ulcer becomes larger or inflamed localization becomes more exact If an ulcer involves the distal end of the stomach the pyloric channel area bizarre symptoms

strictive ulcer type of diet along with a constipating type of medication. Constipation is also frequent in patients who have pyloric obstruction.

HEMATEMESIS AND MELENA

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Gastrojejunal Ulcer

The terms marginal stomal anastomotic jejunal or gastrojejunal ulcer refer to those ulcers which follow surgery for benign ulcerative lesions of the stomach and duodenum in particular gastroenterostomy or gastric resection of the Billroth II type Pain is the most frequent symptom and it is often more severe than that noted with the original ulcer One of the most characteristic symptoms is the shift in location of the pain from the site of the original ulcer The pain shifts downward and to the left In uncomplicated jejunal or stomal ulcer however pain tends to be diffuse and not well localized If perforation or penetration occurs the pain is localized to the left of the umbilicus in the majority of cases Nausea and vomiting are fairly characteristic symptoms This is due to edema which results in obstruction of the stoma Loss of weight is common and diarrhea may occur When severe this may suggest that a gastrojejunal colic fistula is also present (see Chapter 12)

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may occur Nausea and vomiting which are rare in uncomplicated gastric and duodenal ulcers are the most common symptoms in patients with channel ulcer [1] The vomiting is frequent occurring usually within 30 to 60 minutes after a meal When pain is present it is usually relieved by vomiting Typical ulcer pain is not common in these patients and constant pain which lasts days or weeks at a time and requires narcotics for relief may occur Weight loss is also a common finding in pyloric channel ulcer patients

Duodenal Ulcer

Pain is the outstanding symptom of duodenal ulcer Its characteristic features are its quality its rhythmicity periodicity and chronicity It is usually described as a burning aching or gnawing sensation located in the epigastrium frequently just to the right of the midline If the ulcer is small and shallow the pain is poorly localized With an increase in size the pain is more accurately localized and not infrequently the patient can easily cover the site of pain with one finger It is usually steady lasting from 15 minutes to an hour or more It appears from 1 to 4 hours after meals and when present at night it wakens the patient at about 1 A M Nausea and vomiting are uncommon in uncomplicated duodenal ulcer and weight loss is likewise uncommon

If a walled off perforated duodenal ulcer develops the character of the pain changes and radiation of the pain to the back is frequently observed The presenting symptoms of duodenal ulcer can also be hemorrhage or perforation without previous ulcer distress These are discussed in detail in Chapter 12

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DIAGNOSIS

The major part of the diagnosis of peptic ulcer is based upon obtaining a typical history of recurrent ulcer distress The pattern of complaints constitutes the most consistent diagnostic feature of the disease In contrast the physical examination is of much less importance Laboratory studies including gastric analysis and stool examination may be helpful Gastroscopy has a definite although limited value However *the confirmation of the clinical suspicion of the diagnosis will be obtained most frequently from x ray examination* Roentgenologic examination of the stomach and duodenum is particularly important in the patient who gives an atypical history

HISTORY

The patient will usually *report bouts of indigestion which* are intermittent over a number of years and which may become chronic as time goes on Characteristically he will say that the pain comes on several hours after the ingestion of food When an esophageal ulcer is present pain may also occur on swallowing food With gastric ulcer the pain may

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come on sooner but the diagnostic features of esophageal gastric duodenal and marginal ulcers differ little In addition to pain in relation to meals it is not infrequent to get a history of nocturnal pain Ulcer pain is characteristically absent in the morning on arising

With the onset of complications the history becomes more difficult to interpret and the diagnosis of peptic ulcer will depend more on other diagnostic techniques particularly x ray study The patient may present other symptoms than pain Heartburn is sometimes a symptom of peptic ulcer although it is not nearly so characteristic as ulcer pain Occasionally the patient will complain of acid regurgitation or water brash Nausea is an infrequent symptom as is vomiting at least in uncomplicated ulcer Sometimes the initial symptoms may be bleeding with either the vomiting of blood (hematemesis) with coffee ground vomitus or black and tarry stools (melena)

PHYSICAL EXAMINATION

Physical examination of the patient with peptic ulcer yields much less information than a well taken history Indeed in the majority of cases of uncomplicated peptic ulcer the physical examination is entirely negative Sometimes the patient can point to the area where ulcer pain has occurred and occasionally there is tenderness on deep palpation over that area The chief value of the physical examination is to exclude other conditions accompanied by physical findings such as enlarged liver or abdominal masses which might suggest some other diagnosis than peptic ulcer

LABORATORY EXAMINATION

Gastric Analysis

Gastric analysis to test the acidity of the gastric contents is frequently carried out in patients suspected of having peptic ulcers This is particularly true when the ulcer is in the stomach and it is necessary to differentiate it from an ulcerating carcinoma The usual finding is a higher than normal acid in the patient with a duodenal ulcer and slightly lower than normal acid in the patient with a gastric ulcer Patients with carcinoma of the stomach seldom have free acidity Gastric analysis is also of value to determine whether there is gastric retention

It is our practice to carry out a fasting gastric analysis testing a casual specimen to see if free acid is present If free acid is present the test is discontinued If free acid is not present histamine 0 01 mg per kilogram is given and serial samples are taken at 20 minute intervals for the next hour and a half to determine if free acid is present Although still widely used the Ewald meal has little value in the diagnosis and management of the ulcer patient

Stool Examination

It is a good practice to perform stool examinations with ulcer patients Periodically one may find occult blood in the stool However the finding of persistent blood may lead one to suspect an ulcerating carcinoma of the stomach rather than a benign ulcer

Perhaps a word is indicated regarding the technique of performing the stool tests for occult blood In the past it has been observed that false positives could occur if patients

were on a diet high in meat fish or fowl content For this reason patients were frequently placed on a diet excluding such foods for a 3 day period prior to the test We are not sure this is necessary and it is our custom to carry out stool tests for occult blood when the patient is on his regular diet If the test is positive it is repeated the patient being placed on a diet free of meat fish and fowl for 3 days prior to the test Recently there has been some evidence that with the newer tests this can be avoided [1]

Cytologic Examination

It is now possible to study the exfoliated cells from the lining of the stomach While this has no particular application to the diagnosis of peptic ulcer it is useful in excluding the diagnosis of carcinoma when one is dealing with a gastric ulcer It is discussed in detail in Chapter 14

GASTROSCOPY

With the development of the flexible gastroscope gastroscopy has become increasingly valuable in the diagnosis of conditions involving the stomach Obviously it is of little value in the diagnosis of duodenal ulcer but gastric ulcers are frequently in an area where they can be visualized with the gastroscope and this close visualization of the ulcer can make possible a differential diagnosis between an ulcer and an ulcerative carcinoma Other diseases involving the stomach such as gastritis or lymphosarcoma can be differentiated with the gastroscope It is now possible to carry out gastroscopic biopsies and while this technique has not been universally adopted it is of value in some cases [2]

X-RAY DIAGNOSIS

Gastric Ulcer

Gastric ulcers may be divided into two groups those which occur above the incisura angularis and those which occur below the angularis The incisura angularis is an arbitrary point where the line of direction of the lesser curvature changes from a downward to an upward course toward the pylorus The most common site for gastric ulcer is on the lesser curvature between the cardiac orifice of the stomach and the incisura angularis The posterior wall of the lesser curvature is involved more commonly than the anterior wall Benign ulcers can also occur on the greater curvature of the stomach and in or near the pylorus In fact any part of the stomach can be involved [5] For this reason the stomach must be examined through every angle of obliquity in order to determine whether the niche of an ulcer is actually present A crater on the anterior wall may not be seen until the patient is turned in an oblique position so that the crater is then seen as a projection off the lesser curvature Likewise craters involving the posterior wall may not be seen except in the oblique position projecting off the greater curvature Mucosal relief studies using a thin layer of barium are invaluable for recognizing craters involving the central portion of the posterior wall

ULCERS ABOVE THE INCISURA ANGULARIS The fundamental x ray sign of a gastric ulcer is a demonstration of a niche or bud projecting from the stomach The niche is usually rounded and has a comparatively smooth outline In rare instances the contour of the niche may be irregular even though the lesion is benign The niche or bud is indicative

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lesser curvature involving the antrum and pyloric segment may show as niches projecting from the outline of the stomach More commonly they involve the anterior and posterior walls of the stomach and are more difficult to demonstrate than ulcers of the lesser curvature of the pars media They are also more likely to be associated with superimposed alterations of contour as a result of secondary spasm or antral gastritis Direct evidence of a crater is difficult to obtain and more commonly the diagnosis is based on indirect or secondary signs of ulceration The most characteristic sign is persistent spasm of the antral portion of the stomach Changes in motility and delayed emptying may also be noted

Benign ulcer not infrequently involves the pylorus Here one can sometimes note direct evidence of an ulcer manifested by a niche present within the enlarged canal as shown in Figure 15 in the following case

> C R a 40 year old woman had a history of chronic indigestion Duodenal ulcer was diagnosed in 1939 with several recurrences of typical symptoms In 1952 the patient developed epigastric fullness following meals nausea and increasingly frequent vomiting X ray was negative She was placed under the care of a psychiatrist without improvement Symptoms continued until 1954 when x ray revealed a pyloric channel ulcer (Fig 15) There was improvement on intensive therapy

The secondary signs of ulceration are lengthening or distortion of the pyloric sphincter

GASTRIC ULCER AND GASTRIC CANCER DIFFERENTIAL DIAGNOSIS X ray is one of our most valuable techniques for differentiating benign from malignant ulcers (See Chapter 14) Whereas the benign gastric ulcer extends outward from

of the presence of a crater The craters may range from *small or shallow ones which are difficult to demonstrate to* giant ones which result from penetration and the formation of a walled off perforation In addition to the demonstration *of the niche or crater there are indirect signs of ulceration* With gastric ulcers on the lesser curvature side a localized area of spasm which has been termed a spastic incisura may *be seen to involve the wall of the stomach adjacent to* the ulcer This spasm may be so intense as to divide the stomach into a narrow channel producing the hourglass type of stomach Spasm may also be present in the antral region or in the area of the pylorus

Alterations of the rugae about the ulcer may be observed Normally the gastric rugae form parallel lines in the upper portion of the stomach but when an ulcer is present the rugae may radiate toward the crater something like the spokes of a wheel This can be seen best when the stomach is only partly filled with barium

Localized tenderness may sometimes be present over the area of an ulcer This is of little help in the diagnosis of lesions of the upper part of the stomach since this area is inaccessible to palpation Such tenderness is at best only suggestive and is never by itself considered of great diagnostic value Motor disturbances are a common occurrence in peptic ulcer If the ulcer is at or near the pyloric channel it may affect motor function through direct involvement of *the ring Even when the ulcer is situated in the upper two* thirds of the stomach there may be slowing up of the rate of emptying and retention of barium The explanation for this gastric retention is not entirely clear

ULCERS BELOW THE INCISURA ANGULARIS Ulcers of the

the wall of the stomach small ulcerating carcinomas are seen roentgenologically to have a crater which is surrounded by a ridge This is called the meniscus sign The niche of a malignant ulcer may be irregular in outline and tends to be larger than that of the benign ulcer It has been said that lesions larger than 2 5 cm in diameter are more frequently malignant than those that are smaller However neither size nor contour are necessarily reliable criteria A giant gastric ulcer which proved to be benign is shown in Figure 16

There are other suggestions of a malignant lesion One may observe a filling defect which sometimes can resemble spasm A palpable tumor is presumptive evidence of cancer Deformity of the mucosal lining and rigidity of the wall of the stomach are also indicative of a malignant process

Spasm presents a difficult problem to the roentgenologist He must distinguish whether the spasm is secondary to an ulcer or is due to some other disease process involving either the stomach or adjacent organs Frequently this cannot be ascertained with a single examination and recheck studies should be ordered until the diagnosis can be established to the roentgenologist s satisfaction

It should be remembered that although the roentgenologist indicates that the lesion appears to be benign approximately 15 per cent of such lesions ultimately turn out to be malignant For this reason patients with gastric ulcer should be in the hospital where they can be followed carefully with serial x ray examination If upon such examination the crater of the ulcer progressively diminishes and ultimately disappears the lesion is probably benign If the crater remains stationary in size or increases it is probably



Figure 15
X ray showing pyloric channel ulcer

a malignant lesion and surgery is advised Such repeat examinations should probably be made at intervals no longer than 1 to 2 weeks It should be mentioned that certain large gastric ulcers whose base is formed by adjacent structures may not heal by medical management and may present all the characteristics of a malignant lesion but still be benign

Duodenal Ulcer

The x ray study of duodenal ulcer is the most accurate way of diagnosing this condition It supersedes all other means of arriving at the diagnosis of duodenal ulcer Not only is x ray of aid in establishing the diagnosis but serial studies are of value in determining the response to therapy and predicting the development of complications The direct sign of a duodenal ulcer is a demonstration of a deformity in the outline of the duodenum This duodenal abnormality may assume a variety of patterns There are a number of factors which enter into the formation of the duodenal deformity These are niche formation retraction in the region of the niche defect of the curvature opposite the eccentrically placed open pyloric lumen and diverticular dilatations One may see multiple deep lines cutting into and across the duodenal bulb This is most commonly due to duodenal ulcer but may result from extrinsic causes such as postoperative adhesions gallbladder disease and tumor formation

The deformity most commonly observed consists of a pinching in of the sides of the duodenum which ultimately forms the so-called clover leaf pattern wherein the duodenal bulb is segmented into several portions Such clover leaves may be complete or incomplete Not infrequently



FIGURE 16

Left x-ray of a large benign gastric ulcer. Right x-ray of the same ulcer showing healing. (From Barborka *et al.* Reproduced with kind permission of the editor of the *Quarterly Bulletin Northwestern University Medical School.*)

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FIGURE 17
X ray showing a duodenal ulcer

with pressure films one can demonstrate folds which radiate toward a crater (Fig 17)

H B a 66-year old man had intermittent ulcer distress for 15 years Recently he had a change in pattern to nearly constant distress unrelieved by oral anticholinergic agents Physical examination showed epigastric tenderness X ray study demonstrated a large duodenal ulcer crater A penetrating duodenal ulcer was found and gastric resection was performed

These craters are usually located within the first 2 or 3 cm of the duodenal bulb midway between the curvatures The crater represents the x ray counterpart of the ulcer itself Its frequency varies considerably but with improved technique it has been reported that a niche or crater is present in 60 per cent of cases of duodenal ulcer The most common location for a niche is on the lesser curvature border Craters which are present on the anterior or posterior wall are more difficult to demonstrate

Duodenal ulcers beyond the duodenal bulb are rare but occasionally craters are located in the postbulbar area as in this case

M J a 47 year old white woman had long standing polycythemia vera and severe atherosclerosis She developed a postbulbar duodenal ulcer at age 46 recurrent at age 47 (Fig 18)

These can be diagnosed by the presence of a niche and also by the presence of marked narrowing in the second portion of the duodenum adjacent to the niche Alteration in the mucosal relief pattern of the involved area may be present along with localized tenderness

Retraction of the contour of the duodenal bulb at the site



FIGURE 18
X-ray showing a postbulbar crater

of the crater most usually involves the lesser curvature border This is the result of a combination of contraction of longitudinal muscle fibers swelling of the mucosa and actual scar formation On rare occasions a crater may be present without any accompanying abnormality of the contour of the duodenal bulb

Other indirect manifestations of duodenal ulcer may be observed Irritability of the duodenum active gastric peristalsis and reflex gastric spasm are sometimes observed Irritability of the duodenum the most common of these presents problems to the radiologist Because of the irritability the barium passes through rapidly and it is difficult to obtain good films of this area Localized tenderness at the site of the duodenal bulb by itself is of little value in the diagnosis of duodenal ulcer When combined with other evidence of deformity of the duodenum it may in some cases support the original diagnosis It is not necessarily indicative of a duodenal ulcer however as tenderness over the gallbladder may be a normal finding

Some patients with duodenal ulcer show signs of reflex spasm of the stomach An incisura of the greater curvature may be observed rarely but a more common finding is spasm of the pyloric antrum In some of these patients an actual gastritis involving the antral area is associated with duodenal ulcer

When a niche is present it can be used as a criterion of healing of a duodenal ulcer The disappearance of the niche does not necessarily mean that the ulcer has undergone complete healing If the niche remains persistently absent under repeated examinations over a period of time this is further evidence that the ulcer has healed



FIGURE 18
X ray showing a postbulbar crater

sometimes difficult to distinguish from peptic ulcer The distress may be related somewhat to meals and relieved by alkalies in much the same way as in peptic ulcer Among these conditions are atrophic gastritis hypertrophic gastritis carcinoma of the stomach gallbladder disease and conditions involving the pancreas and the intestine Under usual circumstances such conditions can be relatively easily distinguished from peptic ulcer There are two conditions however which present problems at times The first of these is the so called nonulcer dyspepsia

Nonulcer Dyspepsia

Nonulcer dyspepsia or functional dyspepsia is a term used to denote cases in which the clinical symptoms initially suggest peptic ulcer but which show no laboratory or x ray evidence of any organic disease to account for the symptoms With repeated observations and careful x ray study the true diagnosis can usually be established One diagnostic feature differentiating nonulcer dyspepsia and gastritis from ulcer is the failure of the nonulcer patient to achieve complete symptomatic relief Patients with nonulcer dyspepsia or with gastritis are usually improved when placed on ulcer type management but they seldom achieve the complete relief which is so characteristic of ulcer patients On rare occasions one may not be entirely sure whether one is dealing with a functional dyspepsia with pylorospasm or with an ulcer with coexisting pylorospasm Then it is probably best to treat the patient as though he had an ulcer until such time as the diagnosis becomes entirely clear

If a niche cannot be demonstrated x ray gives relatively little aid in determining whether the ulcer has healed Deformities of the duodenal bulb that are due predominantly to the presence of scar tissue tend to be permanent in nature In this situation the deformity indicates that an ulcer has been present in the past but it cannot indicate whether the ulcer is still active

While x ray study of the stomach and duodenum is most valuable it should be kept in mind that there are definite limitations to this procedure Alterations may be observed which are not necessarily indicative of an ulcer these are sometimes called duodenitis Whether this represents an actual inflammation of the duodenum or is a precursor to peptic ulcer is not known Furthermore the interpretation of the x ray findings also presents problems to the roentgenologist His interpretation of the films sometimes depends upon whether the patient s clinical history is consistent with a diagnosis of ulcer Under these circumstances an irritable duodenal bulb and other secondary signs of ulceration may indicate or suggest that the patient has a duodenal ulcer The same findings can be observed in patients who do not have duodenal ulcers The radiologist *therefore depends greatly upon the clinician to supply information* regarding the patient so that the x ray study can be utilized to advantage

DIFFERENTIAL DIAGNOSIS

Many other conditions give rise to epigastric pain or burning heartburn and vomiting and these conditions are

sometimes difficult to distinguish from peptic ulcer. The distress may be related somewhat to meals and relieved by alkalies in much the same way as in peptic ulcer. Among these conditions are atrophic gastritis, hypertrophic gastritis, carcinoma of the stomach, gallbladder disease, and conditions involving the pancreas and the intestine. Under usual circumstances such conditions can be relatively easily distinguished from peptic ulcer. There are two conditions, however, which present problems at times. The first of these is the so-called nonulcer dyspepsia.

Nonulcer Dyspepsia

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Gastric Cancer

As previously mentioned carcinoma of the stomach must always be considered in the differential diagnosis of gastric ulcer This problem is discussed in detail in Chapter 14

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7

MEDICAL TREATMENT

The value of dietary restrictions in the medical management of peptic ulcer has been known for many years. The value of milk and eggs was recognized early by the French clinicians. This was followed, however, by a period in which treatment was influenced by the German physicians who recommended that starvation be carried out in order to rest the stomach. This initially arose as a treatment for bleeding ulcer, but it came to be adopted for all types of ulcer.

Although there were sporadic attempts to influence the starvation treatment, the name most closely identified with present-day treatment is that of Sippy. The Sippy program included 3 to 4 weeks of bed rest and hourly feedings from 7 A.M. to 7 P.M. Powdered alkalies were given every half hour after the last feeding until 10 P.M. Night secretions of highly acid were drained. After a lapse of a few days the program was liberalized to include more milk, cereal, eggs, and other bland foodstuffs. The main principle of the Sippy program was to attempt continuous neutralization of the gastric acid throughout the 24 hour period. Because of

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to exist. In addition, there is an area of lowered resistance from the previous ulcer When the natural history of the disease is studied, one wonders how much recurrences can be influenced by medical treatment Some have even gone so far as to suggest that the main value of medical treatment is to relieve the discomfort and tide the patient over until a spontaneous remission takes place

PHYSIOLOGIC PRINCIPLES

A knowledge of the physiologic principles underlying treatment is essential to good ulcer management. Peptic ulceration results when the eroding factors predominate over defense factors Medical treatment is based on restoring the balance between the eroding and the defense factors This is accomplished in two ways by the control or neutralization of acid gastric juice and by putting the diseased part at rest. Although some claim that one factor is more important than the other it is probable that both are equally important Thus alkalies which are given primarily to neutralize acid can also influence motility Antispasmodics and anticholinergic agents decrease secretion as *well as modify* the motor functions of the stomach It is worthwhile therefore to review the accepted principles of medical management in view of their physiologic justification

Rest and Sedation

Without question the quickest and most certain way to produce symptomatic relief and healing of an ulcer is to put the patient to bed Exactly how bed rest works to achieve

the dangers of systemic alkalosis which were soon recognized [3] searches were made for antacids which would not produce systemic alkalosis Colloidal aluminum hydroxide was introduced in 1922 and other nonabsorbable antacids have been employed since that time

During the last 30 years almost every year has seen a new cure advocated for peptic ulcer Some of these have been combinations of previously employed antacids and antispasmodics whereas others have been totally without pharmacologic basis The chief difficulty with most of these studies is the fact that they were uncontrolled and the investigators attributed improvement to the use of the particular drug or medication whereas in fact the improvement was merely part of the natural history of the disease A more skeptical attitude has prevailed in more recent years

AIMS OF TREATMENT

The aims of treatment are threefold (1) to relieve symptoms (2) to heal the ulcer and (3) to prevent recurrences The relief of symptoms is achieved rather easily by diet and rest However the relief of symptoms is not necessarily tantamount to healing of the ulcer

Complete healing of the ulcer presents a more difficult problem and generally requires prolonged and intensive treatment with bed rest rigid dietary restrictions and the use of adjunct medication It has been estimated that approximately 40 days are necessary for complete healing of an ulcer [4]

The prevention of recurrences is a still more difficult problem inasmuch as the original etiologic factors continue

this end is not known It appears however that the warmth the extra sleep and the relief from tension all contribute to the healing of the ulcer There is also some evidence that the blood supply to the ulcerated area is improved when the patient is in the horizontal position

It is difficult to carry out satisfactory bed rest at home and in general the best results are achieved in the hospital In this environment the patient is separated from his usual worries and responsibilities and has little to concentrate on besides getting well Bed rest in the hospital has other advantages It guarantees the patient a properly executed plan of treatment It also enables the physician to establish rapport with the patient so that treatment may be better individualized It gives the physician an opportunity to teach the patient something about the principles of ulcer treatment which are so essential to maintaining a satisfactory program

Along with prescribing both physical and mental rest and relaxation most physicians give sedative drugs in small dosage Most commonly used is phenobarbital ¼ to ½ grain three to four times a day New long acting preparations of phenobarbital are now available which need be given only once or twice a day The sedative preparation may be incorporated in the antispasmodic or anticholinergic drug

Diet

Dietary treatment has three general purposes (1) to avoid foods which stimulate the flow of acid (2) to administer foods which are effective neutralizers of gastric

acid and (3) to prevent irritation of the ulcer by rough foods

Milk is one of the most important constituents of any ulcer diet and it serves to satisfy all three aims of dietary treatment It does not stimulate gastric secretion its fat content tending to inhibit the flow of acid by stimulating the enterogastrone mechanism it is a good antacid by virtue of its casein content and of course being in liquid form it is not traumatic to the ulcerated area It is usually given as a mixture of milk and cream at hourly intervals but intractable patients may be treated by a continuous milk drip method such as proposed by Winkelstein Winkelstein originally suggested that a mixture of milk and sodium bicarbonate be given continuously throughout the 24 hours for 2 or 3 weeks Subsequently the treatment was modified so that the patient received three bland meals a day and the drip between meals The drip was started 1 hour after the completion of the last meal and continued until 1 hour before the next meal including throughout the nighttime period The gels of aluminum hydroxide and phosphate can also be administered by the drip method

Proper dietary management also excludes foods which are chemical mechanical or thermal irritants Such foods include raw fruits and vegetables which are high in cellulose highly seasoned foods and extremely hot or cold liquids

Attention should be paid to the appearance and palatability of the diet inasmuch as many ulcer patients discontinue their diets because of the monotony Every effort should be made to make the diet interesting to the patient

With patients who are on a restricted diet the use of vitamin supplements particularly vitamin C is desirable A detailed discussion of dietary treatment is presented in Chapter 8 and recipes commonly used in the treatment of peptic ulcer are listed in the Appendix

ANTACIDS

The antacids include the soluble alkalies the nonsystemic antacids and newer preparations such as resins The soluble alkalies such as the Sippy powders were introduced early in the treatment of peptic ulcer Most of the popular available antacids of the systemic alkaline variety are made up of sodium bicarbonate magnesium oxide and calcium carbonate and bismuth The disadvantages of these preparations with the resultant alkalosis have been mentioned

Because of the disadvantages of the soluble alkalies attempts have been made to find insoluble alkalies and such agents as aluminum hydroxide magnesium trisilicate and various combinations have been introduced More recently ion exchange resins have been used for the same purpose

Much effort has been concentrated on reducing the acidity of gastric juice Such a lowering of gastric acidity also indirectly affects the pepsin level inasmuch as pepsin has no significant digestive action above pH 3 5 and is destroyed above pH 7 Antacids reduce gastric acidity by a chemical reaction Complete neutralization of the gastric contents is probably impossible inasmuch as it has been estimated that on the standard Sippy management from twenty five to fifty times as much antacid as is customarily given would be required to neutralize the total daily output

of hydrochloric acid[7] Large quantities of antacids up to ten to twenty times the amount necessary for *in vitro* experiments are necessary in order to lower the free acidity in man for even brief periods of time This is the result of gastric emptying with the loss of antacid from the stomach and also the continued secretion of hydrochloric acid Most authorities feel that total neutralization of acid is unnecessary The nonabsorbable antacids are administered to exclude the possibility of alkalosis

Antispasmodics

The antispasmodics most commonly employed are of the belladonna alkaloid family Atropine is generally used as a standard of comparison for this group It is a tertiary amine compound which exerts a postganglionic parasympathetic depression working on the effector site Its main action is that of an antispasmodic agent although if the dose is increased enough antisecretory effects may follow its use Significant inhibition of gastric secretion of hydrochloric acid is usually accompanied by evidence of atropine toxicity These include blurring of vision dryness of the mouth and tachycardia Mental confusion accompanied by visual and auditory hallucinations may occur occasionally Atropine is sometimes combined with homatropine hyoscyamus or hyoscine Their general action is similar to that of atropine itself Tincture of belladonna containing the mixture of the alkaloids may also be used The synthetic atropine like compounds including Syntropan Trasentine Bentyl and similar substances are useful as antispasmodics but are less effective as antisecretory agents than atropine

Anticholinergic Agents

Recently certain drugs have been introduced which act not only at the effector site but at the ganglionic level blocking cholinergic impulses at both of these places These compounds of which tetraethylammonium chloride (TEAC) is an example are structurally similar to acetylcholine It is thought that they act by replacement of acetylcholine at the autonomic synapse thus excluding it It has been shown following intramuscular injection that TEAC reduces gastric acidity approximately 50 per cent and inhibits gastric motility completely [1] The effect is a temporary one however and the drug is not effective when given orally

The hexamethonium compounds also exert a profound effect upon gastric secretion and motility The use of the hexamethonium compounds is limited by their side effects These consist of postural hypotension as a result of the ganglionic blockade blurring of vision dryness of the mouth and constipation

The most promising development in the field of anticholinergic drugs has been the combination of the amino alcohol ester structure with the quaternary ammonium structure of tetraethylammonium chloride which has resulted in a new series of compounds of which Banthine is the best known These compounds seem to incorporate the pharmacologic actions of both atropine and the tetraethylammonium compounds They appear to have an inhibitory effect upon gastrointestinal motility gastric secretion and mucosal engorgement As these compounds seem to be the most promising developments in ulcer

therapy for many years they are discussed in detail in Chapter 9

Restriction of Coffee, Alcohol, and Tobacco

It is known that caffeine induces a secretion of gastric juice high in acid and low in pepsin In addition it may cause hyperemia of the gastric mucosa Clinical observations indicate that caffeine in the form of caffeine-containing beverages exerts a harmful effect upon the symptoms of an ulcer It is questionable whether they have any part in the causation of the ulcer but nonetheless most physicians feel that ulcer management is improved by the elimination of such beverages

Alcohol also produces a gastric juice high in acidity and as a matter of fact has been used as a test meal for gastric secretion For this reason it is generally recommended that alcoholic beverages be curtailed, if not eliminated in patients who have active ulcers

The action of tobacco on the stomach is less clear In addition to *nicotine tobacco and tobacco smoke contain tars* and other toxic substances not very definitely identified Smoking relaxes the tone of the stomach and in some persons produces a diminution of appetite While it is generally conceded that it is desirable to curtail or eliminate smoking in practice this is a difficult problem It is generally held that better ulcer management is achieved if the patient can discontinue smoking [3]

Psychotherapy

Although there is still disagreement on what role psychological factors play in the formation of an ulcer almost

ANTICHOLINERGIC AGENTS

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those connected with occupation is the most important single factor in preventing recurrences They feel that those situations which are likely to produce a recurrence can be predicted Precautionary measures should be taken to prevent recurrences under stress Dietary control should be made more strict and supplemented by antacids sedatives and anticholinergic agents This program should be continued for the duration of the stressful period

There is still some disagreement on the best way in which long term management should be carried out There are some Illingworth for example who feel that the patient should not be advised to make peace with his stomach modify his way of life and avoid all causes of stress and worry It is his opinion that the ulcer patient cannot abide by such advice and that attempting to follow such a program will rob the patient of all joy in living

Most physicians would be more inclined to agree with Sullivan and McKell who feel that the important factor in dealing with this problem is the education of the patient He must understand that in order to avoid recurrent abdominal pain he must modify his habits In bringing about such a change in his patient the physician must be able to convince him of the wisdom of the change He should be taught that he is a more productive individual if he remains in a healthy state and takes annual vacations and long weekends and finds other outlets for his energy than if he pursues his tasks relentlessly without a break Such treatment must of necessity be individualized It is our feeling that the patient should be encouraged to live as actively as his health permits

It is essential that the patient know when to consult his

all agree that psychotherapy is of value in treatment Inasmuch as it has been shown that the secretory and motor activities as well as the blood supply to the stomach can be influenced by the emotions it is reasonable to assume that improvement in the emotional factors may cut down secretion motility and hyperemia Sympathetic understanding of the patients problems is also of value in calming apprehension and relieving anxiety There is no necessity for formal psychotherapy at the hands of a psychiatrist for the average patient Good informal psychotherapy can be carried out by the practitioner who is possessed of common sense A good physician patient relationship will enable the physician to uncover the mental and emotional conflicts and stresses which are not deep seated Much can be accomplished by correction of these superficial conflicts particularly if the patient understands that adjustment of these problems will contribute greatly to the successful management of his disease Sometimes a change in employment or occupation may be necessary to remove a recurring conflict Separation from outside responsibilities such as committee work and other community efforts may be necessary

It should be remembered that neurotic symptoms are no more common in the ulcer patient than in the general population and in general ulcer patients make light of their symptoms While they may be anxious worried and somewhat tense they usually carry on until their distress prohibits them from doing so

Sullivan and McKell who have made an extensive study of the personality of ulcer patients feel that recognition of the external precipitating emotional situations particularly

those connected with occupation is the most important single factor in preventing recurrences They feel that those situations which are likely to produce a recurrence can be predicted Precautionary measures should be taken to prevent recurrences under stress Dietary control should be made more strict and supplemented by antacids sedatives and anticholinergic agents This program should be continued for the duration of the stressful period

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It is essential that the patient know when to consult his

physician In the case of the duodenal ulcer patient Hussar[16] has suggested that the patient call the physician (1) if symptoms recur and do not respond promptly to management (2) if unusual symptoms appear or if the usual symptoms are of unusual severity (3) *if recurrences come* on frequently (4) if there is any vomiting of bloody or coffee ground material (5) if bloody or tarry stools are observed and (6) if sudden unexplained weakness occurs In the case of a gastric ulcer the patient should be instructed to call his physician whenever any symptoms reappear

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8

DIETARY MANAGEMENT

Dietary management is fundamental to the treatment of the ulcer patient. The objects of dietary management are to avoid foods which stimulate acid, to administer foods which neutralize hydrochloric acid, and to avoid irritation of the ulcer.

BASIC FACTORS IN DIETARY MANAGEMENT

The important factors in dietary management of peptic ulcer are: (1) a nutritionally adequate diet, (2) frequent small feedings, (3) avoidance of mechanically and chemically irritating foods, (4) avoidance of foods which stimulate gastric secretion, (5) the use of protein foods, (6) the use of fat foods, and (7) the use of vitamins and minerals.

NUTRITIONALLY ADEQUATE DIET

The diet for peptic ulcer should be adequate, although feedings may be small in bulk and at frequent intervals. It is important that the diet be balanced, with proper propor

tions of proteins carbohydrates fats minerals and vitamins The estimated minimum daily requirements as compared to the amounts of essential food factors furnished by the usual ulcer diet are shown in Table 1 As can be seen first stage management is inadequate in protein iron and frequently in vitamins A B and C Second stage management is inadequate in iron and niacin whereas ambulatory ulcer management furnishes all the necessary nutrients

Frequent Small Feedings

Small feedings at frequent intervals are generally prescribed The object here is to maintain food within the stomach throughout the waking period and provide for more adequate neutralization of the hydrochloric acid which is formed As the dietary program becomes liberalized the number of hourly feedings is shortened so that there are three main meals with three interval small feedings

Avoidance of Mechanically and Chemically Irritating Foods

Irritating foods should be avoided in ulcer diets as it has been shown that they tend to aggravate the ulcerated condition Foods containing fibers and sharp seeds are omitted entirely from ulcer diets Likewise chemical irritants such as spices or highly seasoned foods should be avoided

Avoidance of Foods Which Stimulate Gastric Secretion

Foods which stimulate gastric secretion such as meat extractives concentrated acid fruits coffee tea and caf

TABLE 1

COMPARISON OF NUTRITIONAL YIELDS OF NORMAL ADULTS AND ANALYSIS OF DIETS FREQUENTLY USED IN THE TREATMENT OF PEPTIC ULCER

	Carbohydrate (Gm)	Protein (Gm)	Fat (Gm)	Calories	Calcium (Gm)	Iron (Mg)	Vit A (IU)	Thiamin (Mg)	Riboflavin (Mg)	Niacin (Mg)	Ascorbic Acid (Mg)
Requirements for Normal Diet											
Man (154 lbs or 70 Kg)											
Sedentary	—	70	—	2400	1.0	12.0	5000	1.2	1.8	12.0	75
Physically active	—	70	—	3000	1.0	12.0	5000	1.5	1.8	15.0	75
Woman (123 lbs or 56 Kg)											
Sedentary	—	60	—	2000	1.0	12.0	5000	1.0	1.5	10.0	70
Physically active	—	60	—	2400	1.0	12.0	5000	1.2	1.5	12.0	70

Approximate Composition of Ulcer Regimen †

First stage ulcer management											
a 2 oz whole milk 2 oz cream	81 0	51 0	216 0	2181	1 9	1 8	5910	0 6	2 8	1 8	18
b 3 oz whole milk 1 oz cream	86 0	55 0	144 0	1560	2 0	1 9	5893	0 7	2 9	1 9	19
c 4 oz whole milk	90 0	51 0	72 0	1221	2 1	1 5	2850	0 7	3 1	1 8	18
d 4 oz skimmed milk	90 0	51 0	18 0	738	2 1	1 8	—	0 7	3 2	1 8	18
Second stage ulcer management	165	80	210	2900	1 6	10	12 460	1 0	2 5	5 2	51
Ambulatory ulcer management	220	90	150	2590	2 4	14	10 700	1 9	3 3	12 7	91

National Research Council Recommended Daily Dietary Allowance (1948 rev)

† Tables of Food Composition in Terms of Eleven Nutrients U S Department of Agriculture Miscellaneous Publication No 572 1945

TABLE 1

COMPARISON OF NUTRITIONAL NEEDS OF NORMAL ADULTS AND ANALYSIS OF DIETS FREQUENTLY USED IN THE TREATMENT OF PEPTIC ULCER

	Carbo hydrate (Gm)	Pro tein (Gm)	Fat (Gm)	Cal ories	Cal cium (Gm)	Iron (Mg)	Vit A (I U)	Thia min (Mg)	Ribo flavin (Mg)	Nia cin (Mg)	Ascor bic Acid (Mg)
Requirements for Normal Diet											
Man (154 lbs or 70 Kg)											
Sedentary	–	70	–	2400	1 0	12 0	5000	1 2	1 8	12 0	75
Physically active	–	70	–	3000	1 0	12 0	5000	1 5	1 8	15 0	75
Woman (123 lbs or 56 Kg)											
Sedentary	–	60	–	2000	1 0	12 0	5000	1 0	1 5	10 0	70
Physically active	–	60	–	2400	1 0	12 0	5000	1 2	1 5	12 0	70

Approximate Composition of Ulcer Regimen †

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a 2 oz whole milk 2 oz cream	81 0	54 0	216 0	2484	1 9	1 8	8910	0 6	2 8	1 8	18
b 3 oz whole milk 1 oz cream	86 0	55 0	144 0	1860	2 0	1 9	5895	0 7	2 9	1 9	19
c 4 oz whole milk	90 0	54 0	72 0	1224	2 1	1 8	2850	0 7	3 1	1 8	18
d 4 oz skimmed milk	90 0	54 0	18 0	738	2 1	1 8	—	0 7	3 2	1 8	18
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feine containing carbonated beverages along with alcohol should be eliminated or greatly curtailed

Protein Foods

Protein foods such as milk and eggs are desirable because of their high neutralizing ability Cheese milk powders gelatin and gelatin desserts all are rich in protein and do not contain the secretory stimulating agents found in meats Protein foods including protein digests have been employed in the treatment of peptic ulcer It is questionable whether this dietary program has any advantage over the traditional programs providing the patient does not stay on a restricted diet too long

Fat Foods

Fats are useful in the treatment of peptic ulcer because they inhibit gastric secretion and gastric motility They also furnish energy because of their high caloric content and small bulk The most commonly used fatty food is cream which is given in half and half proportions in the initial stages of ulcer management

Vitamins and Minerals

Many ulcer diets are deficient in vitamins and minerals This is particularly true of both the vitamin B group and vitamin C It is considered good practice to give supplemental vitamins orally or parenterally when patients are on restricted ulcer type diets

APPLICATION OF DIETARY PRINCIPLES

Although each patient presents a different problem in dietary management the general principles of dietary therapy of ulcer remain the same [1]

First Stage Ulcer Management

The patient whether in the hospital or at home in bed is first started on Diet I the first stage ulcer management diet This diet contains 81 Gm of carbohydrate 54 Gm of protein and 216 Gm of fat with a total of 2484 calories First stage ulcer management starts with the giving of a 4 ounce mixture (120 cc) of equal parts of milk and cream every hour on the hour commencing at 7 A M and continuing through 9 P M or later if necessary Under first stage ulcer management in Table 1 we have outlined three possible variations from the 4 ounce half and half mixture If fewer calories are desired or there is an intolerance to cream possible variations of the amounts of cream or fat in the total 4 ounce mixture are suggested in diets *b* *c* or *d* (see Table 1) In certain instances the patients may prefer a 3 ounce or 90-cc feeding every hour on the hour If so the mixture would be 1 ounces of whole milk and 1 ounces of cream or two thirds milk one third cream which would be 2 ounces of whole milk and 1 ounce of cream or just 3 ounces of whole milk or 3 ounces of skimmed milk Irrespective of whether one chooses a 3 or 4 ounce feeding attention should be called to the nutritional inadequacies of first stage ulcer management

Whatever diet or procedure is selected in first stage ulcer management it should be on the basis of the severity of

Diet I

FIRST-STAGE ULCER MANAGEMENT

Carbohydrate 81 Gm protein 54 Gm fat 216 Gm total calories 2484

Suggested distribution of the total food allowance for 1 day

Feeding at	*Food*	*Quantity*	*Antacid at*
7 00 A M	Milk	2 oz	
	Cream	2 oz	
			7 30 A M
8 00 A M	Milk	2 oz	
	Cream	2 oz	
			8 30 A M
9 00 A M	Milk	2 oz	
	Cream	2 oz	
			9 30 A M
10 00 A M	Milk	2 oz	
	Cream	2 oz.	
			10 30 A M
11 00 A M	Milk	2 oz	
	Cream	2 oz.	
			11 30 A M
12 00 NOON	Milk	2 oz	
	Cream	2 oz	
			12 30 P M
1 00 P M	Milk	2 oz	
	Cream	2 oz	
			1 30 P M
2 00 P M	Milk	2 oz	
	Cream	2 oz.	
			2 30 P M
3 00 P M	Milk	2 oz	
	Cream	2 oz.	
			3 30 P M

DIET I (*continued*)

Feeding at	*Food*	*Quantity*	*Antacid at*
4 00 P M	Milk	2 oz	
	Cream	2 oz	
			4 30 P M
5 00 P M	Milk	2 oz	
	Cream	2 oz	
			5 30 P M
6 00 P M	Milk	2 oz.	
	Cream	2 oz	
			6 30 P M
7 00 P M	Milk	2 oz	
	Cream	2 oz.	
			7 30 P M
8 00 P M	Milk	2 oz	
	Cream	2 oz	
			8 30 P M
9 00 P M	Milk	2 oz	
	Cream	2 oz	

symptoms of the ulcer First stage ulcer management is given only to patients under hospital care or at home at bed rest Occasionally when for good reasons the patient s activities cannot be restricted either in a hospital or at home or for brief periods following a recurring episode of ulcer distress the second stage ulcer management may be advised The diets on first stage ulcer management provide smaller quantities of vitamins and iron than meet the daily nutritional needs During this first stage ulcer management patients should therefore receive vitamin supplements and iron

Treatment in each case may be individualized The adoption of any rigid form of treatment for every case is unwise

If a patient is progressing well under a certain adequate regimen he should be permitted to continue on it for an ample period The tendency to curtail the period of treatment or to make premature additions to the diet or to cater to the whims of the patient often results in subsequent failure Foods capable of causing chemical mechanical or thermal irritation should be excluded for a year or longer The patient should not lose weight under the regimen in fact he should be able to gain weight This can always be controlled during Diet III the ambulatory regimen by altering the interval feeding substances half milk half cream or by the addition of cooked cereals served with cream and sugar butter olive oil custard junket and simple desserts

For some patients during the first stage ulcer management after 6 to 10 days of treatment or even earlier the hourly introduction of food gives rise to gastric disturbances so that some modification of the timing of feedings is necessary It may be best to double the intervals between the feedings of milk and cream that is to have these feedings taken every 2 hours from 7 A M to 9 P M rather than every hour and to have the antacids taken on the hour midway between the feedings of milk and cream Each feeding however is increased to 5 or 6 ounces to maintain proper nutrition and the amount of the alkali when used gradually is increased so as to neutralize the acid Ordinarily the first stage ulcer management is used for about 6 to 8 days depending on the location and type of ulcer and the response of the patient to treatment If the patient responds satisfactorily and becomes symptom free in this period of time he is ready to be placed on Diet II for second stage ulcer management

Second Stage Ulcer Management

The second stage ulcer management diet contains 165 Gm of carbohydrate 80 Gm of protein and 210 Gm of fat with a total of 2870 calories This diet is inadequate in iron niacin and ascorbic acid The milk and cream feedings are kept up as per schedule in this diet but the total of each feeding is reduced from 4 to 3 ounces Small meals are substituted for the milk and cream at 8 A M noon and 6 P M These three small meals consist of strained cooked cereals egg or egg substitutes a small baked potato dry white toast butter cream soups and simple desserts such as custards Jello or junket rice or tapioca pudding prune whip and Bavarian cream made from the bland fruit juices

After about 1 week on second stage ulcer management provided the patient is still comfortable and his distress is controlled he should be able to start Diet III the ambulatory ulcer diet Generally this point is reached in about 2 to 3 weeks after beginning the first stage ulcer management

Ambulatory Ulcer Management

This diet contains 220 Gm of carbohydrate 90 Gm of protein and 150 Gm of fat with a total of 2590 calories This is a bland diet and is adequate in all the essential nutrients to meet the daily recommended requirements of a normal adult When a lower caloric intake is indicated milk may be substituted for the cream in the diet The diet may be increased in calories by adding butter or more cream The meals are served at 8 A M noon and 6 P M The hourly feeding schedule is stopped and midmorning midafternoon

Diet II

SECOND-STAGE ULCER MANAGEMENT

Carbohydrate 165 Gm protein 80 Gm fat 210 Gm total calories 2870

Suggested distribution of the total food allowance for 1 day

Feeding at	*Food*	*Quantity*	*Gm*	*Antacid at*
7 00 A M	Milk	1½ oz	45	
	Cream	1 oz	45	
				7 30 A M
	Breakfast			
8 00 A M	Cereal (strained and cooked)	½ cup	105	
	Egg	1	50	
	Dry white toast	1 slice	30	
	Butter	1 square	10	
	Cream	¼ cup (2 oz)	60	
	Sugar	2 tea spoons	10	
	Beverage – Coffee substitute			
9 00 A M	Milk	1½ oz	45	
	Cream	1½ oz	45	
				9 30 A M
10 00 A M	Milk	1 oz	45	
	Cream	1 oz	45	
11 00 A M	Milk	1 oz	45	
	Cream	1 oz	45	
	Luncheon			
12 00 NOON	Creamed soup			
	Milk	¼ cup (2 oz)	60	
	Cream	¼ cup (2 oz)	60	

DIET II (*continued*)

Feeding at	Food	Quantity	Gm	Antacid at
	Vegetable puree	cup	100	
	Dry white toast	1 slice	30	
	Butter	1 square	10	
	Dessert	1 serving	100	
1:00 P.M.	Milk	1 oz	45	
	Cream	1 oz	45	
				1:30 P.M.
2:00 P.M.	Milk	1½ oz	45	
	Cream	1½ oz	45	
3:00 P.M.	Milk	1 oz	45	
	Cream	1 oz	45	
				3:30 P.M.
4:00 P.M.	Milk	1½ oz	45	
	Cream	1 oz	45	
5:00 P.M.	Milk	1 oz	45	
	Cream	1 oz	45	
				5:30 P.M.
	Dinner			
6:00 P.M.	Egg or egg substitute	1	50	
	Potato, baked	1 small serving	75	
	Dry white toast	1 slice	30	
	Butter	2 squares	20	
	Dessert	1 serving	100	
7:00 P.M.	Milk	1 oz	45	
	Cream	1 oz	45	
				7:30 P.M.
8:00 P.M.	Milk	1 oz	45	
	Cream	1 oz	45	
				8:30 P.M.
9:00 P.M.	Milk	1½ oz	45	
	Cream	1½ oz	45	

and bedtime feedings are given at 10 A.M., 3 P.M., and 8 or 9 P.M. These feedings contain varying proportions of a glass of milk and cream, whole milk or skimmed milk, dependent upon the desire of the physician to alter the total caloric intake.

DIET III

AMBULATORY ULCER MANAGEMENT

Carbohydrate 220 Gm., protein 90 Gm., fat 150 Gm., total calories 2590.

Suggested distribution of the total food allowance for 1 day

Feeding at	*Food*	*Quantity*	*Gm.*	*Antacid at*
				7:30 A.M.
	Breakfast			
8:00 A.M.	Stewed fruit	1 small serving	75	
	Cereal (cooked)	½ cup	105	
	Egg	1	50	
	Dry white toast	1 slice	30	
	Butter	1 square	10	
	Cream	½ glass scant	90	
	Orange juice	½ glass (3 oz.) diluted with equal amount of water	90	
	Sugar	2 teaspoons	10	
	Beverage — Coffee substitute			
				9:30 A.M.
10:00 A.M.	Milk	¾ glass	150	
	Cream	¼ glass	50	
				11:30 A.M.

DIET III (*continued*)

Feeding at	*Food*	*Quantity*	*Gm*	*Antacid at*
		Luncheon		
12:00 NOON	Egg or egg substitute	1	50	
	Potato or substitute	1 small serving	75	
	Vegetable purée	1 serving	75	
	Dry white toast	1 slice	30	
	Butter	1 square	10	
	Stewed fruit	1 small serving	75	
	Milk	1 glass	200	
				1:30 P.M.
3:00 P.M.	Milk	¾ glass	150	
	Cream	¼ glass	50	
				5:30 P.M.
		Dinner		
6:00 P.M.	Creamed soup			
	Milk	¼ glass	50	
	Cream	¼ cup	60	
	Vegetable purée	[illegible] cup scant	75	
	Meat	1 small serving (1½ oz.)	45	
	Potato	1 small serving	75	
	Vegetable purée	1 serving	75	
	Dry white toast	1 slice	30	
	Butter	2 squares	20	
	Milk	1 glass	200	
	Dessert	1 serving	100	
				7:30 P.M.
8:00 or 9:00 P.M.	Milk	¾ glass	150	
	Cream	¼ glass	50	
				9:30 P.M.

If the patient is symptom free after 1 month on the ambulatory diet, vegetables need not be pureed if they are well masticated.

and bedtime feedings are given at 10 A.M., 3 P.M., and 8 or 9 P.M. These feedings contain varying proportions of a glass of milk and cream, whole milk or skimmed milk, dependent upon the desire of the physician to alter the total caloric intake.

Diet III

AMBULATORY ULCER MANAGEMENT

Carbohydrate 220 Gm., protein 90 Gm., fat 150 Gm., total calories 2590.

Suggested distribution of the total food allowance for 1 day

Feeding at	*Food*	*Quantity*	*Gm.*	*Antacid at*
				7:30 A.M.
	Breakfast			
8:00 A.M.	Stewed fruit	1 small serving	75	
	Cereal (cooked)	½ cup	105	
	Egg	1	50	
	Dry white toast	1 slice	30	
	Butter	1 square	10	
	Cream	½ glass scant	90	
	Orange juice	½ glass (3 oz.) diluted with equal amount of water	90	
	Sugar	2 teaspoons	10	
	Beverage — Coffee substitute			
				9:30 A.M.
10:00 A.M.	Milk	¾ glass	150	
	Cream	¼ glass	50	
				11:30 A.M.

TABLE 2 (*continued*)

riced boiled potatoes Also plain buttered noodles macaroni rice and spaghetti

Fruit juices
Three ounces of strained citrus fruit juice diluted with an equal amount of water daily also fruit nectars—grape apple peach pear apricot cherry prune and pineapple

Desserts
Plain cakes (angel food sponge and pound) plain cookies Bavarian cream blancmange custard floating island Jello vanilla ice cream ices junket rice cornstarch and tapioca puddings prune apricot graham whip rennet gelatin

Sweets
Sugar in moderation jelly strained cranberry jelly

Beverages
Coffee substitutes Kaffee Hag Sanka Postum milk malted milk milk shakes evaporated or condensed milk butter milk

Condiments
Salt in moderation

Soups
Strained cream of asparagus carrot celery pea potato spinach string bean and oyster soup

Vegetables
Whole cooked or canned asparagus tips carrots and beets
Peas
Spinach
Squash
String and wax beans
Tender lettuce

Fruits baked canned or stewed
Apples
Apricots
Royal Anne cherries
Peaches
Pears
(all without core skins or seeds)
Puree of dried fruit

Fruits ripe raw
Bananas
Avocados
Pears
Peaches

Peptic Ulcer

Later in the management with the patient well controlled any one of the following combinations may be indulged in as the interval between meal and the bedtime feedings chocolate milk and cream malted milk or milk shake eggnog made with milk and cream ice cream without fruits or nuts cream soup or a serving of a dessert or cereal if desired as outlined in Table 2

TABLE 2

TYPICAL FOODS USED IN THE TREATMENT OF PEPTIC ULCER

Cereal
- Cream of Wheat
- Farina
- Rice
- Strained oatmeal
- Cornmeal
- Cornflakes
- Puffed rice
- Rice Krispies
- Rice flakes
- Pablum

Bread
- Plain white bread toast or Melba toast
- Zwieback

Fats
- *Butter or substitute and cream as desired*

Eggs
- Prepared in any way but fried – soft cooked poached soufflé baked omelet scrambled in milk

Cheese
- Cottage
- Philadelphia cream
- Mild American
- Cheddar (American) used in cooking

Meat
- Tender or scraped beef
- Baby veal Liver
- Lamb Sweetbreads
- Chicken Oysters
- Fish Bacon
- (These may be roasted broiled stewed or creamed)

Potato and substitutes
- Baked buttered creamed escalloped mashed

TABLE 3 (*continued*)

Sardines
Lobster
Crab

Broths
Bouillon
Beef cubes
Beef broth
Chicken broth

Fried or greasy foods
Fried meats or chicken
Fried vegetables
Fried eggs (fried in ham or bacon fat)
Nuts

Raw vegetables
All

Cooked vegetables
Kohlrabi
Parsnips
Old beets
Sauerkraut
Corn on cob
Cabbage family
Onions and garlic

Raw fruits
Apple
Pineapple
Orange
Tomato
Grapefruit
Lemon juice
Fresh cherries

Spices or highly seasoned foods
Steak sauces
Rich gravies and stews
Chili sauce
Pickles and olives
Vinegar
Mustard
Horseradish
Catsup
Worcestershire sauce

Spiced or pickled vegetables or fruits
All

Beverages
Coffee and tea
Coca Cola or other caffeine containing beverages
Carbonated beverages
Very hot or very cold beverages
Alcohol

DIETARY MANAGEMENT IN HEMORRHAGE

DEVELOPMENT OF DIETARY TREATMENT

The old routine medical management of bleeding ulcer was comprised of bed rest nothing by mouth morphine

It is possible after a month on the ambulatory diet particularly if there is need for more protein in the diet to increase the meat servings to 2 or 3 ounces again varying and choosing the type of meat as outlined in Table 2

The ambulatory ulcer management diet is continued after the patient is dismissed from the hospital He should be cautioned not to depart from instructions regarding the type of foods to be allowed and those to be avoided as outlined in Tables 2 and 3 It is important that the milk and cream mixture or one of the combinations of interval feedings suggested be continued midway between the three meals and at bedtime for an indefinite period of time It may also be advisable at times to give some milk (½ glass) when the patient first awakens in the morning Emphasis should be placed upon the punctuality of all diet and medical treatment Many times slight distress may be controlled by food especially milk or milk and cream

TABLE 3

TYPICAL FOODS TO AVOID IN THE TREATMENT OF PEPTIC ULCER

Coarse whole grain cereal
- Krumbles
- Shredded wheat
- Bran
- Bran flakes
- Ralston
- Wheatena

Hot or hard breads
- Ry Krisp
- Cracked wheat bread
- Corn bread
- Griddle cakes
- Pancakes
- Gingerbread
- Hot biscuits
- Wholewheat bread
- Coarse rye bread

Meat and fish
- Pork
- Corned beef
- Ham
- Salmon

7	4 drams per dose total 4 eggs also 1 soft boiled egg every 4 hours total 4 eggs	2 oz per dose total 25 oz	40 Gm	70 Gm with boiled rice 100 Gm in 3 doses
8	4 drams per dose total 4 eggs also 1 soft boiled egg every 4 hours total 4 eggs	1 oz per dose total 28 oz	40 Gm	70 Gm with boiled rice 100 Gm in 8 doses
9	4 drams per dose total 4 eggs also 1 soft boiled egg every 4 hours total 4 eggs	3 oz per dose total 1 qt	40 Gm	Beef same rice 200 Gm zwieback 40 Gm in 2 portions
10	4 drams per dose total 4 eggs also 1 soft boiled egg every 4 hours total 4 eggs	Add chopped cooked chicken 50 Gm also butter 20 Gm	40 Gm	Beef same rice 200 Gm zwieback 40 Gm in 2 portions

11 and 12 Interval of feeding made 2 hours milk given in 6 oz doses with oz raw egg butter increased to 0 Gm and various additions made as detailed above

From Friedenwald and Ruhl

TABLE 4

LENHARTZ DIET AS MODIFIED BY LAMBERT

Day	*Egg*	*Milk*	*Sugar*	*Scraped Beef*
1	2 drams per dose, total 2 eggs	4 drams per dose, total 6 oz		
2	3 drams per dose, total 3 eggs	6 drams per dose, total 10 oz		
3	oz per dose, total 4 eggs	1 oz per dose, total 13 oz	20 Gm added to eggs	
4	5 drams per dose, total 5 eggs	1 oz per dose, total 1 pt	20 Gm added to eggs	
5	6 drams per dose, total 6 eggs	14 drams per dose, total 19 oz	30 Gm	
6	7 drams per dose, total 7 eggs	2 oz per dose, total 22 oz	40 Gm	36 Gm in 3 doses

7	4 drams per dose total 4 eggs also 1 soft boiled egg every 4 hours total 4 eggs	2 oz per dose total 25 oz	40 Gm	70 Gm with boiled rice 100 Gm in 3 doses
8	4 drams per dose total 4 eggs also 1 soft boiled egg every 4 hours total 4 eggs	1 oz per dose total 28 oz	40 Gm	70 Gm with boiled rice 100 Gm in 8 doses
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1 and 12 Interval of feeding made 2 hours milk given in 6 oz doses with 1 oz raw egg butter increased to 0 Gm and various additions made as detailed above

[illegible]

and an icebag to the epigastrium In 1904 Lenhartz[5] recommended the use of frequent protein feedings in the treatment of ulcer to assist in the neutralization of acid and to facilitate ulcer healing However he was rather cautious in the administration of early feedings using only 4 teaspoons of milk and 2 teaspoons of egg each hour during the first day (Table 4) Carlson observed that in the healthy animal the fasting stomach is not a resting or quiet stomach In criticism of the fasting plan of treatment for bleeding ulcer Alvarez and Carlson[6] in 1936 pointed out that while efforts were directed towards not disturbing the clot the delicate fibrin was being exposed to the strongly acid unbuffered gastric juice

Andresen departed from the preliminary starvation period in the management of peptic ulcer hemorrhage In 1927 he advocated the immediate feeding of a gelatin lactose mixture (Table 5) In 1934 Meulengracht first

TABLE 5

LONG ISLAND COLLEGE HOSPITAL DIET FOR PATIENTS WITH GASTRIC HEMORRHAGE

Character of Feedings

		Oz	*Gm*	*Calories*
Gelatin solution	Gelatin	1	30	123.0
	Lactose	3	90	360.0
	Juice of 1 orange			47.5
	Water	32	1000	
Gruel mixture 2	Cereal gruel (oatmeal barley or cornmeal)	16	500	338.5
	Milk	14	420	290.8
	Cream	4	120	435.9
	Lactose	3	90	360.0

TABLE 5 (*continued*)

		O	*Gm*	*Calories*
Gruel mixture 2	Cereal gruel (same)	12	350	227 5
	Milk	32	1000	692 0
	Cream	4	120	458 9
	Lactose	4	120	480 0

Schedule of Feedings

	O	*Total Calories*
First and second day feed every 1 hours		
Gelatin solution	4	947 2
Third day feed every 1 hours		
Gelatin solution	4	
Gruel 1	5	1365 4
Fourth day feed every 1½ hours		
Gelatin solution	5	
Gruel 1	5	1499 3
Fifth and sixth day feed every 1 hours		
Gelatin solution	6	
Gruel 2 †	6	3600 0
Seventh and eighth day feed every 2 hours		
Gelatin solution	6	
Gruel 2 †	6	3600 0

From LaDue

† Add to gruel mixture at each feeding one of the following 3 oz cereal 1 soft poached egg custard or Jello

recommended the immediate use of a high caloric purée diet (Table 6) along with alkalies antispasmodics and iron in the treatment of ulcer hemorrhage

Much credit is due Meulengracht for popularizing the principle of prompt feeding an approach which had been appreciated previously by Lenhartz and Andresen Many

and an icebag to the epigastrium In 1904 Lenhartz[8] recommended the use of frequent protein feedings in the treatment of ulcer to assist in the neutralization of acid and to facilitate ulcer healing However he was rather cautious in the administration of early feedings using only 4 teaspoons of milk and 2 teaspoons of egg each hour during the first day (Table 4) Carlson observed that in the healthy animal the fasting stomach is not a resting or quiet stomach In criticism of the fasting plan of treatment for bleeding ulcer Alvarez and Carlson in 1936 pointed out that while efforts were directed towards not disturbing the clot the delicate fibrin was being exposed to the strongly acid unbuffered gastric juice

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	Juice of 1 orange			47 8
	Water	32	1000	
Gruel mixture 2	Cereal gruel (oatmeal barley or cornmeal)	16	500	338 5
	Milk	14	420	290 8
	Cream	4	120	158 9
	Lactose	3	90	360 0

tient while still fulfilling the principles of prompt feeding.

Modern Dietary Management

Following hemorrhage from a peptic ulcer, food and drink should be withheld for a variable period in order to determine the degree and extent of the hemorrhage. Complete rest, both physical and alimentary, is essential. The loss of nutrition during this short preliminary fasting period is negligible compared with the importance of overcoming shock, if present, and determining what type of management is proper for each individual case.

The history, the clinical appearance of the patient, and the laboratory studies should enable one to classify a hemorrhage as mild to moderate or severe. This is an important decision, since severe hemorrhages may indicate potential surgical candidates.

Feeding is out of the question for patients admitted in shock until they have recovered from the vascular collapse. If the patient is nauseated or is vomiting, the diet should be withheld; with the disappearance of nausea or vomiting, feeding may be initiated.

In cases of apparent mild hemorrhage without nausea or vomiting, particularly in those patients under 45 years of age, hourly feedings of 1 to 2 ounces of milk and cream mixture may be given at once. Ordinarily, after 3 or 4 days the patient is taking from 3 to 4 ounces of milk each hour twelve to fourteen times during the day and being given feedings during the night if awake. Fifty or 100 mg. of ascorbic acid may be added to one of the feedings each day, or given parenterally. After the fifth day, or as soon

Table 6

MEULENGRACHT DIET

First day

A M	6 00	White bread and butter tea
	9 00	Oatmeal with milk white bread and butter
P M	1 00	Pureed vegetable (peas carrots) mashed potato tea white bread and butter
	3 00	Cocoa or tea
	6 00	Mashed potato pureed vegetable custard white bread and butter tea

Second day and thereafter

A M	6 00	Tea white bread and butter
	9 00	Oatmeal with milk white bread and butter
P M	1 00	Cream of vegetable soup (peas potatoes carrots string beans asparagus) boiled or mashed potatoes pureed vegetables (peas carrots asparagus) cooked strained fruit plain rice or tapioca pudding junket Jello plain milk pudding chocolate or cornstarch pudding white bread and butter tea
	3 00	Cocoa or tea
	6 00	Cream cheese or eggs (soft boiled or poached) boiled or mashed potatoes or cereal with *milk and sugar*
	6 00	Pureed vegetables dessert from above list white bread and butter

authorities question the wisdom of the routine use of the bulky meals of the Meulengracht diet however particularly in seriously ill patients and various alternative diets have been suggested as being more easily consumed by the pa

tient while still fulfilling the principles of prompt feeding

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as bleeding has ceased the dietary management of the average patient is followed as outlined for the second stage of uncomplicated peptic ulcer

A prompt feeding program of some form is usually rec*ommended as soon as the degree and extent of hemorrhage* is determined and it appears not to be an uncontrollable massive hemorrhage A feeding program is desirable in order to provide needed nutrition to serve as buffer for gastric acidity and to keep enough food in the stomach to avoid hunger contractions *The modified Sippy diet is used* extensively and is more suited to the treatment of hemorrhage In otherwise uncomplicated cases the addition of meat to this regimen on or after the fourth day in the form of broiled scraped beef balls tender ground beef lamb or veal may be desirable Ordinarily the patient is allowed to be up sometime during the third week and therefore may begin the ambulatory ulcer management diet at that time *Such a dietary program is carried out for a period of 6* months or longer

DURATION OF DIETARY MANAGEMENT

Dietary management should obviously be continued in a fairly strict sense until it is thought that the ulcer has healed Clinical judgment and experience are required to gauge *the duration of time necessary for the healing of a* peptic ulcer In most cases of uncomplicated ulcer healing will begin when therapy is begun and will be generally complete within 6 weeks

When hemorrhage has occurred it has been suggested that strict dietary management be continued for 3 weeks

after symptomatic relief has been obtained and the stools are negative for occult blood X rays may be taken at this time to determine whether a crater is still present If a crater is present strict dietary restrictions should be followed until complete healing occurs

The recommendations in regard to dietary treatment of gastric ulcer without hemorrhage are similar Strict diet should be followed until the ulcer is completely healed When dealing with gastric ulcers the x ray checkups should be carried out at more frequent intervals than with other types of ulcers

If the patient remains symptom free an ambulatory diet should be followed extremely carefully for a period of 12 to 18 months Periodic checkups should be carried out for the next 3 to 5 years Should a recurrence develop dietary management should be resumed in a strict fashion

Diet may also be of value in preventing recurrences Althausen has indicated that recurrences may be related to dietary indiscretions It is to the patient s advantage that rather strict dietary restrictions be carried out for 6 months following a symptomatic recurrence If the patient is symptom free at the end of the 6 month period the program can be liberalized somewhat but he should continue to follow an ambulatory diet program for another 12 to 18 months

The skill of the physician is particularly important in encouraging the patient to maintain dietary restrictions Of course it is necessary to individualize the type of handling with various patients Some patients have to be told never to eat certain foods whereas other patients can be trusted to indulge in them only occasionally Care must be taken not to overemphasize the dietary aspects of treatment

while neglecting the other aspects of preventing recurrences which have been mentioned previously It is unlikely that dietary restrictions alone prevent recurrences and certainly monotonous and unappetizing meals are unlikely to do so Our present viewpoint is that peptic ulcer is largely a constitutional disorder associated with psychological factors such as anxiety frustration and suppressed resentment As Hunt[1] has expressed it it is a disease more of an emotional origin related to conditions of strain and worry than a disease of dietary deficiencies and excesses

The result of this point of view has been the use of more liberal diets for ulcer patients paying attention to the appearance and variety of the diet while still following good principles of dietary management Recipes for foods commonly used in ulcer diets are listed in the Appendix A more detailed presentation can be found in Jordan and Hibbens book *Good Food for Bad Stomachs*[1]

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7 ANDRESEN A F R *J A M A* 89 1397 1927

In addition to its intrinsic innervation the gastrointestinal tract is supplied with extrinsic nerve fibers derived from both branches of the autonomic nervous system The parasympathetic innervation is supplied by the vagus nerve while the sympathetic innervation is supplied by the splanchnic nerves The main function of the autonomic nervous system is to maintain the stability of the internal environment[1] The control of these functions by the autonomic nervous system is reflex in nature and primarily involuntary It is however influenced by emotional situations Although in the past it was thought that the vagus nerve served primarily to stimulate the motor and secretory functions of the stomach and that the sympathetic system had inhibitory actions this was not entirely correct Wolf and Wolff have observed that emotionally charged life situations can produce hyperactivity of either division of the autonomic nervous system The usual gastrointestinal effects noted after stimulation of the parasympathetic system are an increase in gastrointestinal motility and an increase in secretion The anticholinergic agents which are parasympathetic depressants tend to exert an inhibitory effect on gastric secretion and gastrointestinal motility

PHARMACOLOGY

The anticholinergic agents or cholinergic blocking agents block acetylcholine which is the chemical mediator of nerve impulses in the parasympathetic nervous system Since acetylcholine is the transmitter of nerve impulses at the ganglionic synapses as well as at the postganglionic effector site an anticholinergic agent may act at either or

9

ANTICHOLINERGIC DRUGS

The anticholinergic drugs include a variety of substances which interfere with the effects of acetylcholine and are therefore depressants of the parasympathetic nervous system While a number of drugs have anticholinergic activity our discussion is limited to the belladonna alkaloids the synthetic analogues of atropine and to the newer quaternary ammonium compounds which have been introduced for the treatment of peptic ulcer The initial reports regarding the quaternary ammonium compounds in the treatment of ulcer were extremely enthusiastic With the passage of time controlled studies have been carried out and we are now in a better position to assess the value of these agents in comparison to the older drugs in the management of peptic ulcer

The rationale of the use of these agents is based on the theory that parasympathetic overactivity may have an important part in the development and maintenance of a peptic ulcer It is thought therefore that drugs which selectively depress the parasympathetic system may have considerable usefulness in the treatment of ulcer

action at the ganglionic level are also similar chemically and are classified as quaternary amines

Tertiary Amines

Atropine the classic parasympathetic depressant is a tertiary amine The pharmacologic action of atropine and the related belladonna alkaloids hyoscyamine and scopolamine *is at the postganglionic effector site* Ganglionic transmission is not affected by clinically useful dosage The main action of atropine upon the gastrointestinal tract is in lessening motor activity which results from overactivity of the parasympathetic system [a]

Atropine is also used in combination with the other bella donna alkaloids such as hyoscyamine and scopolamine The pharmacologic effects of these preparations resemble those of atropine alone Unfortunately there is no localization of the cholinergic blockade produced by atropine and related belladonna alkaloids and the sphincter muscle of the iris the ciliary muscles of the lens and the salivary glands are affected as well as the gastrointestinal tract Because these side effects limited the usefulness of the atropine group of compounds research was concentrated on developing drugs which would be more specific in their action The earliest phase of this research consisted in the development of tertiary amines which were simple analogues of atropine incorporating various groupings of the molecule into amino alcohol esters such as Trasentine and Pavatrine Other drugs of this group include Syntropan Bentyl and Centrine Most of these compounds appear to have rather slight action on the gastrointestinal tract and as a group their clinical effectiveness has been disappointing (Fig 20)

both of these sites Ganglionic blockade can also be produced by interfering with acetylcholine transmitted nerve impulses at the sympathetic ganglia resulting in sympatholytic effects The cholinergic blockade may involve all

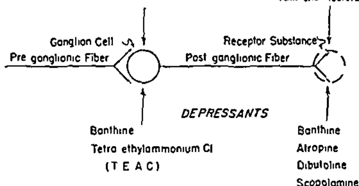


FIGURE 19

Schematic representation of the pharmacology of drugs influencing the parasympathetic nervous system

the organs innervated by the cholinergic system or it may be more selectively related to the gastrointestinal tract

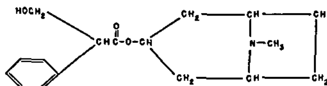
The cholinergic blocking agents can be classified into two groups depending upon whether they act primarily at the postganglionic effector site or at the ganglion between the post and preganglionic fibers (Fig 19) The older drugs including atropine and its analogues acted mainly at the *postganglionic effector site* They are quite similar chemically all being tertiary amines The newer drugs having

action at the ganglionic level are also similar chemically and are classified as quaternary amines

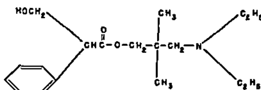
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Atropine the classic parasympathetic depressant is a tertiary amine The pharmacologic action of atropine and the related belladonna alkaloids hyoscyamine and scopolamine is at the postganglionic effector site Ganglionic transmission is not affected by clinically useful dosage The main action of atropine upon the gastrointestinal tract is in lessening motor activity which results from overactivity of the parasympathetic system [3]

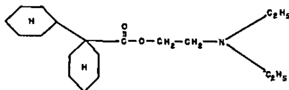
Atropine is also used in combination with the other belladonna alkaloids such as hyoscyamine and scopolamine The pharmacologic effects of these preparations resemble those of atropine alone [4] Unfortunately there is no localization of the cholinergic blockade produced by atropine and related belladonna alkaloids and the sphincter muscle of the iris the ciliary muscles of the lens and the salivary glands are affected as well as the gastrointestinal tract Because these side effects limited the usefulness of the atropine group of compounds research was concentrated on developing drugs which would be more specific in their action The earliest phase of this research consisted in the development of tertiary amines which were simple analogues of atropine incorporating various groupings of the molecule into amino alcohol esters such as Trasentine and Pavatrine Other drugs of this group include Syntropan Bentyl and Centrine Most of these compounds appear to have rather slight action on the gastrointestinal tract and as a group their clinical effectiveness has been disappointing (Fig 20)



ATROPINE



SYNTROPAN

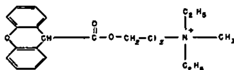


BENTYL

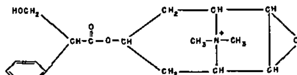
FIGURE 20
Chemical structure of representative tertiary amines

QUATERNARY AMINES

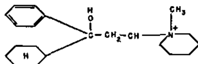
Because of the limitations of the tertiary amines the pharmacologists turned to the preparation of quaternary amines The first of these were the simple quaternary ammonium salts such as tetraethylammonium and hexamethonium compounds Both of these agents are effective paren



BANTHINE



PAMINE



TRICYCLAMOL

FIGURE 21

Chemical structure of representative quaternary amines

terally in decreasing gastric secretion and motility but their ganglionic blockade with resultant postural hypotension has limited their usefulness in the treatment of peptic ulcer

The combination of the amino alcohol ester structure with the quaternary ammonium structure of tetraethylammonium has resulted in compounds such as Banthine The chemical structures of these quaternary amines are quite similar (Fig 21)

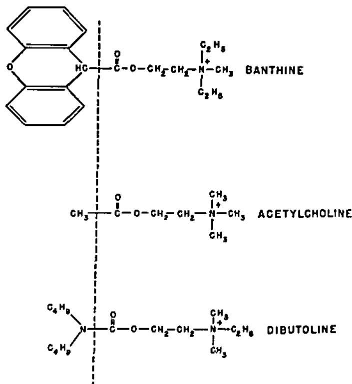


FIGURE 22
Chemical structure of Banthine acetylcholine and Dibutoline

The pharmacologic effects of the quaternary amines differ somewhat from the effects produced by the tertiary amines The quaternary amines have little direct relaxing effect upon the muscle in comparison with the tertiary amines *However the quaternary amines are more active* in blocking cholinergically induced activity in the intestine than the tertiary amines Because of this their clinical effectiveness is increased The quaternary amines are less

readily absorbed than the tertiary amines with the result that oral toxicity is decreased while intravenous toxicity is increased From the combination of these effects a more favorable balance appears to result between gastrointestinal activity and side effects The lessened side effects permit attainment of blood concentrations sufficient to inhibit gastric secretion of hydrochloric acid as well as motor activity of the gastrointestinal tract

There is a marked similarity in structure between the new quaternary amines and acetylcholine (Fig 22) This structural similarity is thought to be related to their mode of action as it has been postulated that the blocking agents work by preventing acetylcholine from being attached to the cell The agents thus become attached to the site usually occupied by acetylcholine Some degree of selectivity of action might be expected as a result of this blocking activity and this appears to be the case with the newer anticholinergic agents

EVALUATION OF NEW ANTICHOLINERGIC DRUGS

The cholinergic blocking agents of the quaternary type available include Banthine Antrenyl Prantal Pamine Dibutoline Darstine Pro Banthine Lorine Tricoloid Malcotran Novatrine Piptal Monodral and Pathilon Elorine and Tricoloid are identical compounds and Malcotran and Novatrine are brands of homatropine methyl bromide The major pharmacologic action of these compounds in the usually employed dosage is at the effector site although in larger dosage blockade is produced at the ganglionic level

Effect on Gastric Secretion

The more potent anticholinergic drugs inhibit gastric secretory activity with reduction in both secretory volume and hydrochloric acid This effect is measured with the basal gastric secretion technique The response following oral administration of these drugs is variable and anacidity is seldom produced with the currently available drugs unless rather high dosage is employed Even though they interfere with the cholinergically induced secretion these drugs do not completely block the cephalic phase of gastric secretion [8]

The ideal antisecretory drug has been characterized pharmacologically as one which selectively inhibits the parasympathetic ganglia and/or the terminal nerve endings preferably only those ganglia or nerve endings associated with gastric secretion without appreciable adrenergic blockade or curariform activity [9] The clinical requirements of such a drug are that it can be safely administered is capable of suppressing secretion for a long period of time after oral administration and is without disagreeable side effects

The comparative evaluation of the antisecretory effects of these agents presents many problems The methods used for evaluating the inhibitory effects differ There is also the problem of knowing what are equivalent doses of the compounds Furthermore the therapeutic value of an anticholinergic agent depends not only upon inhibition of secretion but also upon the absence of untoward side reactions Many observers feel that the depressant effect on motility is equally as important as the antisecretory effect

Sun and Shay have studied the effects of atropine and

the new anticholinergic agents on the suppression of gastric secretion in relation to their side effects. Anacidity was not produced without accompanying dryness of the mouth with any of the agents studied. They felt that the optimum effective–minimal toxic dose was that dose which suppressed gastric secretion and produced dry mouth without blurring of vision.

The earlier drugs introduced were not very satisfactory antisecretory agents. Although Banthine and Prantal were observed to have antisecretory effects following intramuscular administration, they are without significant antisecretory effects when given by the oral route. The antisecretory effects of oral Antrenyl are also variable and not significant.[3, 8]

Dibutoline is a choline derivative which is used only parenterally. It is capable of reducing the volume of gastric secretion when given in dosage of 40 mg every 3 hours.[14] The responses to histamine and insulin stimulated secretion are also partly suppressed at this dosage level. Because of the necessity for parenteral administration it is certainly not an ideal antisecretory agent.

Darstine has been effective in inhibiting acid secretion in dogs. Subsequent clinical studies failed to demonstrate any antisecretory effect when the drug was administered in recommended dosage,[6] although it was well tolerated. Antisecretory effects without significant side effects have been observed when Darstine was given in higher dosage.

The more recently synthesized agents are more active inhibitors of gastric secretion. Kirsner and Palmer concluded from their studies that the most potent oral antisecretory agents were Pamine, Pro-Banthine and Monodral. Elorine

appeared to be less potent having variable effects on secretion Sun and Shay[10] also carried out comparative studies with the newer antisecretory agents Their results showed that Pro Banthine Darstine and Pamine were more effective than atropine Banthine or Malcotran in suppressing gastric secretion

Pro Banthine tricyclamol homatropine methyl bromide Pathilon and Piptal have been evaluated using the basal gastric secretion technique With Pro Banthine tricyclamol Piptal and homatropine methyl bromide significant depressant effects on secretory volume and hydrochloric acid were observed The drugs having the most favorable ratio between antisecretory effects and side effects were Piptal and tricyclamol[1]

Effect on Gastrointestinal Motility

The effect on gastrointestinal motility is more pronounced and less variable than that on secretion Significant depressant effects have been observed with all of the drugs studied The motor depressant effects have been evaluated using two techniques In the first a meal of barium sulfate was given and its rate of passage through the stomach and small intestine was observed The test was then repeated after the patient had received the anticholinergic agents Using this technique Chapman et al compared the effects of Banthine with those of tincture of belladonna and a placebo Banthine caused a delay in gastric evacuation and a decrease in the movement of the barium along the intestine but no changes were observed with either the placebo or the tincture of belladonna Similar effects have been noted with the other cholinergic blocking agents

When the drugs are given parenterally either intramuscularly or intravenously all gastrointestinal motor activity of a peristaltic nature can be inhibited

The use of intragastric and small bowel balloons has also aided in the study of the motor effects of the anticholinergic agents When an intragastric balloon is connected to a recording kymograph it has been observed that anticholinergic agents such as Banthine inhibit the type 2 antral contraction waves These are the waves which produce gastric evacuation

Other Effects

It has been reported that a decrease in engorgement of the gastric mucous membrane occurs after administration of these agents [4] As might be expected undesirable side effects may follow the use of these compounds The side effects are related to their pharmacologic structure and resemble those which follow the administration of atropine Side effects as a result of ganglionic blockade can be noted also The most common side effects are visual and salivary disturbances but difficulty in urination tachycardia constipation lassitude dermatitis and a curariform action have been observed on occasion [5]

USE IN PEPTIC ULCER

Indications

There is general agreement that the anticholinergic agents are useful in the symptomatic treatment of peptic ulcer Their administration is usually followed by prompt relief of ulcer distress This relief is frequently so striking

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injection of the drug at periodic intervals usually every 6 hours or by intramuscular injection each time ulcer distress recurs The latter method is preferable as it enables the physician to determine more accurately the clinical im provement in the patient In such instances the pain of ulcer can be relieved in a few minutes by injecting the drug either intramuscularly or intravenously

A small number of patients fail to respond symptomati cally to conventional therapy supplemented by anticholin ergic drugs whether given by the oral or parenteral route It is usually found that such patients have perforated walled off ulcers and that conservative therapy is of little value Sometimes partial relief of ulcer pain is observed with the epigastric or visceral component being relieved while the somatic or back component is unchanged

The anticholinergic agents appear to be useful in the management of active peptic ulcer Their most striking clini cal effect is relief from ulcer pain This appears to be due primarily to their effect on gastroduodenal motor function Because the pain is relieved so promptly it cannot be used as an index to healing of the ulcer When a crater is present this can be followed However craters frequently cannot be demonstrated in patients having symptoms of an active duodenal ulcer It has been claimed that some of these compounds decrease the healing time of peptic ulcers but there are no good statistical data to support this contention

Interim Phase

Dietary restrictions and other treatment are recom mended during the quiescent or interim phase in an at

that initially it was recommended that some of these drugs could constitute the sole treatment for peptic ulcer It soon became apparent that this attitude was hazardous to the patient and it is now recommended that the anticholinergic drugs be used as adjunct treatment to conventional medical management

Active Phase

Anticholinergic drugs are probably not necessary for all patients having ulcer distress They are not necessary for the patient having occasional mild symptoms In such a situation routine medical management without the use of the anticholinergic agents is probably sufficient However in the more severely ill patient where symptoms persist in spite of good ambulatory medical management the addition of an anticholinergic agent to the therapeutic regimen is frequently followed by gratifying symptomatic relief Such relief is not necessarily indicative of the healing of the ulcer and silent bleeding has been observed in patients who were on continuous anticholinergic drug therapy For this reason it must be emphasized again that the anticholinergic drugs in this phase constitute only adjunct therapy to other forms of management such as rest diet sedation and antacids

For those patients who do not respond promptly to ambulatory treatment hospitalization is indicated The usual dietary sedative and antacid program should be prescribed Parenteral therapy with the anticholinergic drugs may be used in conjunction with the usual methods of treatment The parenteral route can be utilized either by intramuscular

As all three of these factors appear to play some role in the pathogenesis of pain and perhaps in the pathogenesis of the ulcer itself the use of anticholinergic agents appears to be based on sound pharmacologic grounds

Contraindications

The role of these drugs in the treatment of the complications of ulcer is still somewhat controversial It is certain that the drugs are contraindicated in the presence of organic pyloric stenosis Although it is possible that they might have some theoretical value in the treatment of the bleeding patient because of their effect in decreasing motility and acidity we feel that their use in this situation is hazardous Certainly the likelihood of any contemplated surgical intervention contraindicates their use This is also true for patients suspected of having a perforation who will require surgical intervention

There are other prohibitions to the use of the anticholinergic agents Because of their effect on the bladder producing an atony they are contraindicated in the presence of prostatic obstruction They should be avoided in patients with glaucoma

Dosage

The dosage of the cholinergic blocking agents varies because the compounds are not equally potent milligram for milligram The usual dose per day of the oral medication is 4 to 8 tablets For the average patient 5 tablets a day are recommended 1 given prior to each meal and 2 at bedtime If the patient is having more severe distress or is refractory to this dosage 2 tablets may be given four times

tempt to eliminate or minimize recurrences The value of the anticholinergic drugs in the prevention of recurrences is being assessed

Controlled clinical studies have been carried out with one of these compounds In one study 250 patients with duodenal ulcers having a well defined pattern of recurrence were followed for a 2 year period [6] All patients were treated in the conventional manner the one variation in treatment being that half the patients received 0 4 mg of atropine sulfate four times a day while the other half received a similar tablet of 100 mg of Banthine four times a day Throughout the course of the study neither the physician nor the patients were aware of the nature of the medication It was found that the patients who had been taking Banthine were symptomatically improved and had somewhat fewer and milder recurrences than those who were taking atropine The recurrence rates were high in both groups being 75 per cent in the Banthine group and 90 per cent in the atropine group for the mean observation period The incidence of complications and the necessity for surgery were identical at the end of the 2 year period It was concluded therefore that although symptomatic improvement frequently accompanied the use of these agents it did not appear that the eventual course of the disease was altered

It appears that recurrences cannot be prevented and the incidence of complications probably cannot be influenced by the use of these agents in long term management of the ulcer patient Nonetheless their use is rational since they promote a more favorable environment for healing by reducing secretion hypermotility and mucosal engorgement

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a day The amount that can be taken depends upon the therapeutic effectiveness and the side effects of the compound

Parenteral preparations are available for some of these agents The dose is usually considerably smaller than that of the corresponding oral form Side effects are more common following parenteral administration than following oral administration

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10

OTHER THERAPEUTIC ADJUNCTS

In addition to dietary restrictions and rest there are other therapeutic adjuncts useful in the treatment of peptic ulcer The antispasmodic and anticholinergic agents which decrease secretion as well as modifying motor functions of the stomach were discussed in the previous chapter The other group of compounds commonly employed are the gastric antacids which are used to decrease the quantity of hydrochloric acid in the stomach Hormones and hormone like agents have also been used in the treatment of ulcer Physical measures such as irradiation of the stomach are considered by some to be useful adjuncts in ulcer management

In addition to these adjuncts which have been studied in considerable detail new therapeutic approaches are being tried which have not been evaluated clinically It is possible that some of these may ultimately prove to be useful

ANTACIDS

An antacid may be defined as a substance capable of lowering the acidity of the gastric contents This can be accomplished by three different mechanisms The first of these is direct neutralization of hydrochloric acid Compounds which act in this manner are sodium bicarbonate and magnesium oxide The second mechanism whereby antacids act is buffering of the gastric acid which normally has a pH of 1 or 2 Compounds in this class include sodium citrate and magnesium trisilicate The third mechanism combines adsorption of hydrogen ions of hydrochloric acid and partial neutralization of the acid Substances in this class include hydrated aluminum oxide and exogenously supplied gastric mucin

The gastric antacids are important because they constitute one of the largest classes of medicinal substances employed in medical practice and by the laity Their rationale of use is based on the observation that peptic ulcer results from a localized destruction of the mucosa of the gastrointestinal tract which is bathed by gastric juice The healing of the ulcer is necessarily dependent upon counteracting the eroding forces this includes neutralizing or at least buffering gastric acidity for long periods of time Other therapeutic measures such as rest dietary restrictions and antispasmodic drugs and sedatives should be employed at the same time

Gastric antacids may be divided into two categories with respect to their physical characteristics the systemic or soluble antacids and the nonsystemic or insoluble antacids

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produce systemic alkalosis and should not interfere with gastrointestinal digestion An antacid should elevate the pH of the gastric contents to a degree sufficient to ensure not only neutralization of free acid but inactivation of pepsin This is equivalent to raising the pH above 4 The ideal antacid should be able to maintain the pH of the gastric contents at this level for an appreciable period of time without subsequent rebound activity An antacid should not produce either diarrhea or constipation

Types of Antacids

SODIUM COMPOUNDS Sodium bicarbonate is a soluble antacid which was employed in the original Sippy plan of management The average dose was 1 Gm Sodium bicarbonate produces prompt neutralization of hydrochloric acid but is a less effective neutralizer than magnesium oxide or calcium carbonate It is also unable to produce a prolonged buffering effect and may cause gastric distention through the liberation of carbon dioxide For these reasons and because of its tendency to produce systemic alkalosis its use has been largely abandoned in medical practice Sodium citrate and sodium acetate have also been employed in the past but have been discarded because of the development of better antacids that are without danger of systemic alkalosis

POTASSIUM COMPOUNDS Potassium bicarbonate resembles sodium bicarbonate in its action and has the same disadvantages Its use has been largely abandoned

BISMUTH COMPOUNDS Bismuth compounds which include bismuth subcarbonate bismuth subnitrate and bismuth subgallate have been commonly employed in the

Soluble or Systemic

These agents are absorbed readily from the gastrointestinal tract and enter the general circulation Sodium bicarbonate sodium citrate and sodium acetate are all typical members of this class Neutralization after their use is rapid effective but not prolonged There are several disadvantages in the use of systemic antacids The absorption *of sodium ions augments the alkaline reserve of the blood* and alkalosis can follow their use[1] This alkalosis is characterized by headache abdominal pain nausea and vomiting Renal damage can also occur after prolonged use These drugs are reported to stimulate the rebound secretion of gastric hydrochloric acid

Insoluble or Nonsystemic

The nonsystemic antacids contain cations which are poorly absorbed and therefore have no direct effect upon the acid base equilibrium of the blood Examples of this class of antacids include magnesium oxide calcium carbonate and aluminum hydroxide gel

Some of the nonsystemic antacids react chemically with hydrochloric acid to form salts while others merely bind the hydrochloric acid when in an acid medium releasing the chloride when in an alkaline medium

Desirable Characteristics

It has been suggested that the ideal antacid should be palatable and nonirritating to the stomach *It should not* have any toxic or other untoward effects and its action should be confined to the alimentary tract It should not

produce systemic alkalosis and should not interfere with gastrointestinal digestion An antacid should elevate the pH of the gastric contents to a degree sufficient to ensure not only neutralization of free acid but inactivation of pepsin This is equivalent to raising the pH above 4 The ideal antacid should be able to maintain the pH of the gastric contents at this level for an appreciable period of time without subsequent rebound activity An antacid should not produce either diarrhea or constipation [3]

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treatment of ulcer Although they are the basis of some pro prietary antacids they are actually poor antacids and tend to be constipating

CALCIUM COMPOUNDS Calcium carbonate is a nonab sorbable antacid of good neutralizing ability It is sparingly soluble in water and reacts slowly with hydrochloric acid to form calcium chloride The resulting calcium chloride remains for the most part unabsorbed and is excreted in the feces

MAGNESIUM COMPOUNDS Magnesium oxide is an insol uble compound which has been shown *in vivo* to be the most effective neutralizer of hydrochloric acid of all the commonly used antacids [9] It reacts slowly with hydrochloric acid to form magnesium chloride which is converted to magnesium carbonate in the intestine Since magnesium is poorly absorbed magnesium oxide falls in the category of the insoluble antacids The usual dose is 0 6 Gm Because of its laxative effect usually no more than four doses can be given daily without provoking diarrhea Magnesium hydroxide or milk of magnesia resembles magnesium oxide and is given in doses of 4 cc in a manner similar to mag nesium oxide Magnesium carbonate acts like magnesium oxide but is a less effective antacid

Magnesium trisilicate is a nonsystemic antacid with ef fective adsorptive properties When mixed with gastric contents magnesium trisilicate forms magnesium chloride and colloidal silicon dioxide The customary dose is from 0 5 to 1 0 Gm every four hours Magnesium trisilicate is frequently used in conjunction with aluminum hydroxide to combat the constipating quality of aluminum hydroxide gel Tribasic magnesium phosphate is similar in action to tri

basic phosphate of calcium and is used in a similar manner

ALUMINUM COMPOUNDS Aluminum hydroxide is a non absorbable antacid that does not disturb electrolyte balance It may be used as a powder in tablet form or as a liquid containing a suspension of hydrate of aluminum hydroxide Nonreactive aluminum hydroxides as in Gelusil and Alu minoid react on hydrochloric acid solely as physical agents Nonreactive aluminum hydroxide gel appears to be less ef fective as an antacid than reactive aluminum hydroxide gel While reactive aluminum hydroxide (Amphojel and Cream alin) is identical in composition it reacts chemically with hydrochloric acid Neutralization of gastric acidity by alu minum hydroxide is not great[8] but it does have demulcent properties similar to those of magnesium trisilicate thus tending to protect the ulcerated area

There are disadvantages to aluminum hydroxide the chief one being its constipating action The usual dose is from 5 to 10 cc of the liquid gel every 1 or 2 hours The medication is also available as tablets which must be chewed prior to swallowing Aluminum phosphate resembles aluminum hy droxide but does not have the phosphate diverting action of aluminum hydroxide The dose is the same

Aluminum has also been combined with amino acids to form other compounds such as aluminum glycine prepara tions and dehydroxyaluminum aminoacetate Dehydroxy aluminum aminoacetate gives immediate and prolonged neutralization of gastric acidity Combinations of aluminum hydroxide magnesium trisilicate and mucin are also avail able

Rossett and Rice[9] have worked out an ingenious device for *in vitro* evaluation of the efficacy of some of the fre

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quently used antacids The antacids are added to a beaker containing hydrochloric acid which represents the hydrochloric acid of the stomach The continuous secretion of hydrochloric acid is simulated by a continuous addition of hydrochloric acid to the beaker A stirrer mixes the antacid with the hydrochloric acid and a continuous recording pH meter measures the pH over a period of several hours Using this technique it was found that the tablet preparations of aluminum hydroxide compounds in general were much less effective than equivalent amounts of liquid gel in maintaining the pH above 3 Only one aluminum compound dehydroxyaluminum aminoacetate in tablet form was more effective than aluminum hydroxide or an equivalent amount of its liquid counterpart It was also found that aluminum hydroxide gel combined with milk of magnesia was a more effective antacid than aluminum hydroxide gel alone In practice the amount of milk of magnesia was varied to permit control of the bowel movements

GASTRIC MUCIN Gastric mucin is obtained by digesting the linings of hogs stomachs with pepsin and hydrochloric acid and precipitating the mucin from the supernatant fluid The mucin is administered in the form of a bulk powder the average dose being 2 5 Gm While it is of value in healing experimentally produced ulcers it is a relatively poor antacid in the dosage recommended

ANION EXCHANGE RESINS Anion exchange resins are insoluble inert plastic substances which when given in finely dispersed form are capable of removing acids from solution by direct adsorption These anion exchange resins have been used as antacids They are essentially nontoxic but in large doses may produce nausea The dose is 0 5 Gm at

hourly intervals These compounds have been demonstrated to be fairly good antacids but they have the disadvantage of requiring large doses to achieve this effect

PROTEIN HYDROLYSATES Protein hydrolysates have also been used in the treatment of duodenal ulcer They act as antacids having a prolonged buffering activity Their use was suggested by the fact that ulcer diets tend to be low in protein and it was thought that increased amounts of protein might aid in healing the ulcer Beneficial effects have been ascribed to their use but they are not particularly palatable and have not been widely adopted

SODIUM CARBOXYMETHYLCELLULOSE This is a weak salt of a weak organic acid and a strong base which goes into solution slowly passing through a gel stage It is a moderately good antacid and tends to adhere to the wall of the stomach [1] Diarrhea sometimes follows its use The dose is 10 to 20 cc four to six times daily

ADMINISTRATION OF ANTACIDS

There have been many attempts to evaluate the efficacy of the generally used antacids In the original Sippy program the antacid powders were bismuth subcarbonate sodium bicarbonate calcium bicarbonate and heavy magnesium oxide These powders have excellent neutralizing value They were recommended to be given hourly from 7 30 A M until 7 30 P M and at 8 00 8 30 and 9 00 P M The character of the bowel movements was regulated by varying the amount of magnesium powders Because of the fact that sodium bicarbonate is likely to produce alkalosis the original Sippy program has been modified The most

quently used antacids The antacids are added to a beaker containing hydrochloric acid which represents the hydrochloric acid of the stomach The continuous secretion of hydrochloric acid is simulated by a continuous addition of hydrochloric acid to the beaker A stirrer mixes the antacid with the hydrochloric acid and a continuous recording pH meter measures the pH over a period of several hours Using this technique it was found that the tablet preparations of aluminum hydroxide compounds in general were much less effective than equivalent amounts of liquid gel in maintaining the pH above 3 Only one aluminum compound dehydroxyaluminum aminoacetate in tablet form was more effective than aluminum hydroxide or an equivalent amount of its liquid counterpart It was also found that aluminum hydroxide gel combined with milk of magnesia was a more effective antacid than aluminum hydroxide gel alone In practice the amount of milk of magnesia was varied to permit control of the bowel movements

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pounds so that constipation does not present any particular problem. Mixtures of two parts of aluminum hydroxide and one part magnesium trisilicate seem to combine the best features of each of these antacids. Fifteen to 30 cc. of the antacid is given at each dose. If it is inconvenient to use the liquid medication, the preferable antacid in tablet form is dehydroxy aluminum aminoacetate.

HORMONES AND HORMONE-LIKE AGENTS

The activity of almost all the hormones has been studied in relation to peptic ulcer. This subject has recently been critically reviewed by Kirsner.[13] Inhibitory hormones such as enterogastrone and urogastrone have been found to depress secretory activity in the dog, but similar results have not been demonstrated in man. The inhibitory results in dogs followed intravenous injection. Enterogastrone has not been employed intravenously in man, but after oral or intramuscular injection no inhibitory effects on gastric secretion have been observed, and it does not seem to be of value in the treatment of peptic ulcer.[4]

The favorable results obtained with chorionic gonadotropin or with uroanthelone in the treatment of experimental ulcers in dogs have suggested that these preparations might be of value clinically. Symptomatic improvement has been reported in patients treated with uroanthelone derived from human pregnancy urine, but relapses were not prevented. An extract derived from pregnant mares' urine (Kutrol) has been reported to produce favorable clinical results. The more recent observations are less favorable and the ultimate value of uroanthelone remains in doubt.[5]

commonly employed antacids now are calcium carbonate and the nonsystemic magnesium and aluminum antacids

There is considerable difference of opinion as to the choice of the alkali and the dose If an attempt is made to maintain a pH of 3 5 or less it is necessary to follow an hourly or semihourly program similar to that originally recommended by Sippy In this type of program milk and cream are given on the hour during the daytime between meals and antacid powders are given on the half hour throughout the day Palmer [11] recommends calcium carbonate in 2 to 4 Gm doses Strict attention must be paid to the bowels and magnesium carbonate powders must be substituted at times for calcium carbonate to prevent fecal impactions Rossett *et al* [1] have recommended the use of calcium carbonate with magnesium oxide and milk when protein was in the stomach and a mixture of aluminum hydroxide gel and milk of magnesia when the stomach was empty or contained little protein Protein was given in amounts of 100 to 150 Gm daily primarily for its neutralizing value

The problem of prescribing antacid therapy for those patients who are on ambulatory ulcer management is not easily solved Here one must compromise between achieving effective neutralization and not inconveniencing the patient too much We usually follow the practice for ambulatory ulcer management outlined in Chapter 8 In this program the antacids are given a half hour before each meal and an hour and a half afterwards and at any other time the patient has ulcer distress Thus routinely the patient receives six doses per day given at 7 30 9 30 11 30 1 30 5 30 7 30 and 9 30 The antacids most commonly employed are those which combine aluminum hydroxide with magnesium com

to occur if the ulcer is in an active phase with inflammation and edema

Following irradiation gastroscopic changes can be observed These consist of hyperemia edema hemorrhage and exudation Gastroscopic biopsies have shown that coagulation necrosis occurs in the depths of the fundal glands and this is followed by a decrease in gastric acidity to the point of anacidity in some patients

The effects on gastric secretion are variable Permanent achlorhydria is rarely produced and a permanent depression in gastric acidity results in only one third of patients

Palmer and associates have treated approximately a thousand patients by irradiation In all patients it was used as an adjunct to conventional methods of ulcer management It is difficult to evaluate the results of this radiation therapy Palmer and his associates feel that after radiation treatment the incidence of recurrences is reduced although in their experience the most satisfactory results seem to be obtained in gastric ulcer They feel that radiation therapy is a worthwhile adjunct particularly in the refractory ulcer patient Most other workers are less enthusiastic about radiation therapy

EXPERIMENTAL APPROACHES

Many therapeutic agents are being investigated at the present time Active searches are being made for better antacids Considerable research is being carried out in the field of the cholinergic blocking agents and it is probable that better drugs will be forthcoming

The relations of the hormones and hormone like sub

Mention should be made of the relation of the adrenal hormones to ulcer treatment It has been observed that patients receiving ACTH for other conditions have developed flare ups of a previously quiescent ulcer Gray[19] has reported that there is a marked increase in acid production and uropepsin excretion in patients receiving ACTH over a long enough period of time It is possible that this is one of the mechanisms whereby recurrences develop From the practical standpoint certainly the hormones — corticotropin cortisone and hydrocortisone — should be used with caution in patients who have a past history of peptic ulcer It is probably best to give concurrent antacid therapy if these hormones have to be utilized for some other purpose The hormones are of no value in the treatment of the peptic ulcer itself

RADIATION THERAPY

Radiation therapy in peptic ulcer is based on its depressant effect on acid gastric secretion which is thought to aid the process of healing Variable effects may be produced by radiation therapy Radiation directed toward the fundus and body of the stomach may result in healing of the ulcer because of decreased secretion and subsequent decreases in acid peptic activity If radiation is directed to the antrum and is given in too large quantities tissue necrosis and ulceration may develop

Ricketts and Palmer have recommended that total doses of from 1600 to 2400 r be given over a 12 day period Side effects consisting of the usual radiation toxic manifestations may follow the use of radiation therapy This is more likely

to occur if the ulcer is in an active phase with inflammation and edema

Following irradiation gastroscopic changes can be observed These consist of hyperemia edema hemorrhage and exudation Gastroscopic biopsies have shown that coagulation necrosis occurs in the depths of the fundal glands and this is followed by a decrease in gastric acidity to the point of anacidity in some patients [1]

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The relations of the hormones and hormone like sub

stances to the therapy of peptic ulcer are being investigated further The fact that these inhibitory agents have been of value in preventing experimental ulcers in animals and yet without benefit in man is not entirely understood The relation of the adrenal hormones to the development and treatment of ulcer is also being studied To date there is no conclusive evidence that there is any increase in the amount of circulating ACTH in ulcer patients If such were the case it is possible that a compound to inhibit or inactivate ACTH or cortisone might be of value in treatment

The chemical agents which exert a direct depressant effect upon the parietal cells are also being investigated It is possible that future developments will take the line of the use of enzyme inhibiting compounds It has been shown that the carbonic anhydrase inhib tor acetazoleamide (Diamox) inhibits hydrochloric acid secretion without affecting secretory volume (Fig 23) It appears to act by inhibiting the catalytic effect of carbonic anhydrase on the hydration of carbon dioxide Its practical value in the treatment of peptic ulcer has not yet been demonstrated

It has also been postulated that peptic ulcer may result from depletion of the substrate of the several enzyme systems within the stomach In this hypothesis it is thought that carbon dioxide is utilized by the carbonic anhydrase system of the parietal cell and urea by the urease system of the surface cells of the *stomach In ulcer patients it is postulated* that insufficient amounts of urea and sources for carbon dioxide are available Therefore these substances have been supplied to ulcer patients with encouraging results in some instances The general experience so far appears to be that these combinations work as very mild ant*acids but are of*

little value in treating the patient with the refractory ulcer

Therapy which is directed toward altering the body's response to stress is also being investigated. The use of pyrogenic substances derived from polysaccharides of the Sal

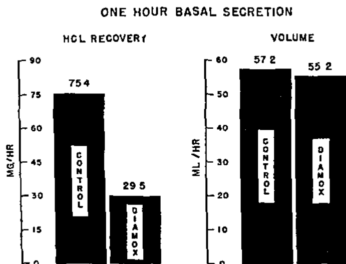


FIGURE 23

Effect of oral Diamox (15 mg per kilogram) on gastric secretion in man

monella organisms is reported to be of value. These pyrogenic substances have been used in the past in the treatment of hypertension and the preliminary results in the treatment of peptic ulcer are encouraging. Controlled studies will have to be carried out before this form of therapy can be evaluated.

Pharmacologic agents which influence the nervous system may be of value. Sedation in the form of barbiturates is

rather standard practice in the treatment of peptic ulcer Recently some new compounds which allay anxiety and produce tranquility have become available One of these is Rauwolfia the active ingredient of which is reserpine This alkaloid which is derived from an Indian plant root is capable of influencing the body and producing a tranquil state It also has cholinergic stimulating activity and in experimental animals stimulates gastric secretion and motility It is possible that this cholinergic stimulating action could be counteracted by combining it with an anticholinergic drug Another nonbarbiturate sedative which is being studied is chlorpromazine (Thorazine) This drug appears to act on the hypothalamus affecting the centers controlling nausea vomiting, sleep and appetite It is possible that it may also represent a useful adjunct in ulcer treatment

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11

PREVENTION OF RECURRENCES AND COMPLICATIONS

It is not easy to evaluate the results of medical treatment in preventing recurrences and complications Uncomplicated peptic ulcer may heal spontaneously or with little treatment and some physicians as a result have advocated a policy of minimal treatment especially early in the course of the disease This was the attitude taken toward the treatment of peptic ulcer during the previous century After the advent of surgical treatment for peptic ulcer the results of treatment both medical and surgical were studied with keener interest so that comparisons might be made between the results of the two types of treatment These studies have made it possible for us to evaluate more critically the results of treatment

One problem which has plagued the attempts to evaluate medical treatment is the *post hoc ergo propter hoc* type of reasoning In this situation improvement which occurs is

ascribed to a given therapeutic regimen disregarding the fact that spontaneous remissions frequently occur Almost every year has seen a new cure being advocated for peptic ulcer as a result of such uncontrolled studies

Controlled studies are necessary to evaluate the results of treatment especially in a disease such as peptic ulcer which follows so variable a course Controlled evaluation of therapy may be set up in two ways In one type of study the patients are divided into two similar groups one group receiving the agent being studied and the other a similar appearing placebo Such a study should be "double blind" neither the patient nor the physician knowing whether the agent or the placebo is being administered A second approach to the problem of evaluating therapy consists in using the past record of the patient as a control for the treatment being evaluated This is not as satisfactory as concurrent parallel studies but it can be combined with the first method to gain additional data Even when experimental studies utilize the paired comparison method it is still difficult to evaluate the results of treatment since evaluation is based primarily upon the subjective response of the patient In addition to comparing the control patients with the treated patients each patient's status after treatment must be compared with his status prior to the initiation of the new treatment A large enough group of patients must be studied long enough to assure that statistically valid conclusions will be drawn

At the end of the treatment period the patient can be evaluated both subjectively and objectively without knowledge of what treatment he received The answers to these questions — Did the patient have fewer or less severe recur

rences? Were complications less frequent? Was the incidence of surgery reduced? – indicate whether the therapeutic agent under study was actually of value [1]

The definition of a recurrence also presents problems Many of the previous studies do not define a recurrence or they give unsatisfactory definitions so that the results of treatment obtained in the different studies are not comparable The most frequent definition given is that a recurrence is a redevelopment of recognizable symptoms of peptic ulcer but without mention of their severity or duration When daily symptom cards (completed by the patient) were used in the evaluation of a therapeutic agent it was observed that most of the patients studied over a 2 year period had several major recurrences a year In addition to the major recurrences which the patients readily recognized as such scattered individual days of ulcer distress occurred almost every month It became necessary to define a recurrence arbitrarily as (1) the recognition on the part of the patient of his usual ulcer distress lasting for a minimum of 5 consecutive days or (2) the development of hemorrhage or perforation or obstruction or (3) the definite x ray evidence of ulcer activity

RESULTS OF TREATMENT

The results of treatment can be evaluated by the effect of treatment upon the immediate symptoms during the acute attack and by its remote results as measured by the incidence of recurrences

The Acute Attack

Rapid relief of symptoms is the rule when patients are placed on careful medical management An ambulatory type of program is frequently sufficient to produce symptomatic relief in the majority of patients If an ambulatory program is not successful even when adjunct therapy in the form of the anticholinergic drugs is used the patient should be hospitalized Hospitalization has the dual advantage of enabling us to carry out more carefully controlled treatment and giving us the opportunity to instruct the patient in the nature of the condition and what measures are necessary for its treatment Symptomatic relief occurs very promptly after admission to the hospital usually within the first 24 hours The majority of patients are symptom free within 2 weeks and only 5 per cent are intractable to medical management in the hospital

The clinical improvement of the patient generally parallels the healing of the ulcer although ulcers may persist for a long period of time without accompanying symptoms Asymptomatic ulceration occurs more frequently with gastric ulcers than with duodenal ulcers and is more common when patients have been on long term anticholinergic drug therapy The healing time of gastric craters in the stomach averages between 4 and 6 weeks Complete healing of the crater occurred within 8 weeks in 136 of the 145 patients followed by Smith and Jordan There was a close correlation between the gastroscopic and the x ray evidence of healing of gastric ulcers

X ray examination for determining the healing time of

rences? Were complications less frequent? Was the incidence of surgery reduced? — indicate whether the therapeutic agent under study was actually of value [1]

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Effect on Recurrences

The clinical course of peptic ulcer differs from that of many other conditions in that it is characterized by long periods of complete or nearly complete freedom from symptoms alternating with shorter periodic recurrences of ulcer distress The results of treatment are therefore both gratifying and disappointing Even though recurrences do occur there are few chronic diseases in which the results of treatment are more definite

In an early study on the results of medical treatment in peptic ulcer Greenough and Joslin observed that 50 per cent of 167 patients studied had good initial results but that the majority developed symptoms later Since that time a number of surveys of the long term results of treatment have been reported These have been reviewed by Althausen[4] and Flood

Long term results of treatment are considered favorable by most physicians even though a recurrence of ulcer symptoms at some time may be anticipated in the majority of patients who have chronic peptic ulcer (See Table 7) Between 10 and 36 per cent of patients will have a recurrence during the first 6 months following a medical cure The incidence of recurrences increases with succeeding years so that at the end of the first 5 years between 46 and 93 per cent of patients will have had one or more recurrences There is some variation in the incidence of recurrences depending on whether the subjects are clinic or private patients the frequency of recurrences appearing to be lower in private patients It is likely that the better results are re

duodenal ulcers does not carry the same precision as with gastric ulcers The healing time is probably the same as with gastric ulcers although again there are wide variations Simon and Boulay[4] have studied the value of the x ray study in assessing the progress of duodenal ulcer treatment A total of 134 patients with duodenal ulcer were studied 63 of these had definite craters 71 had a duodenal cap deformity alone Only 6 of the 63 patients with craters had definite evidence of persistence of the crater at a second or subsequent examination The ulcer crater became smaller as symptoms subsided in most instances but it was often present even though there was a complete remission of symptoms Duodenal cap deformities seldom changed despite change in symptoms Simon and Boulay pointed out that the radiologic method for demonstrating duodenal ulcer is far from foolproof and failure to show a crater in absence of symptoms cannot be taken as an indication of healing Certainly the radiologic evaluation of the disappearance of ulcer craters is a rather crude estimate of ulcer healing The measurement of healing time is further complicated by the technical difficulties of the x ray study and variation in the skills of the individuals performing the examinations

Failure of the patient to follow a rigid regimen is probably the commonest cause of an unsatisfactory initial result It has been found that emotional maladjustment plays a considerable role in the poor results that occur in some patients These same factors appear also to influence the remote results of treatment as measured by the incidence of recurrences

Natvig et al 1943	582	Ward				62%		
		Private	10%					50%
Bockus 1944	246			56%		75%		80%
Krarup 1946	151	Industrial contract	36%		83%			
Raimondi and Cullen 1946	233	Ward		49%	54%	65%	75%	78%
Flood 1948	250	Ward		82%				
Texter et al 1953		Clinic						
		Private						

TABLE 7

INCIDENCE OF RECURRENCES IN PEPTIC ULCER

Authors	Number of Patients	Type of Patients	Period of Observation					
			6 mos	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
Jordan and Kiefer 1932	592	Private		9%	19%	30%	39%	46%
Emery and Monroe 1935	1435	Clinic		79%	84%			93%
Eusterman and Balfour 1936	600	Private				35%		50%
Crohn 1938		Ward		31%		59%	73%	
St John and Flood 1939	225	Ward			65%			78%
Holland and Logan 1941	373	Private			65%	60%	69%	78%

the part of the patient cannot be overemphasized Many patients who have been labeled intractable are merely showing the result of their own failure to co operate or the failure of the physician to utilize the best plan of medical treatment

Specific Measures of Treatment

Special methods of treatment have been utilized in an attempt to prevent recurrences Three specific approaches have been employed in addition to conventional treatment (1) the use of hormones inhibitory in the gastrointestinal tract such as enterogastrone and related substances (2) the use of radiation therapy directed to the stomach and (3) the long term use of the anticholinergic drugs

ENTEROGASTRONE Enterogastrone will delay or prevent the occurrence of gastrojejunal ulcers in approximately 75 per cent of dogs treated with it in which the Mann Williamson operation has been performed but it has not been demonstrated to be of value in preventing recurrences in human ulcer patients It is possible that this difference in response is related to its mode of administration since in the experimental animals it was given intravenously while in human clinical trials it was administered either orally or intramuscularly There is no definite evidence at the present time that either enterogastrone or related similar hormone like preparations are of any value in preventing recurrences of peptic ulcers

IRRADIATION Radiation therapy to the stomach has also been used in an attempt to decrease the incidence of recurrences Ricketts *et al* reported that the incidence of recurrences was lowered following irradiation in patients

lated to the more satisfactory physician patient relation established with private patients

It seems clear that recurrences constitute the major problem in the treatment of peptic ulcer Althausen[6] has studied the inciting causes for recurrences These are physical and mental fatigue emotional disturbances dietary indiscretions and infections especially those which involve the upper respiratory system

PREVENTION OF RECURRENCES

The prevention of recurrences begins with the diagnosis of peptic ulcer This diagnosis should not be made casually because it places upon the patient certain restrictions which may have to be followed for his lifetime After it is definitely established that the patient has peptic ulcer the next step in preventing recurrences is adequate treatment This includes a graduated diet treatment from first stage to second stage and finally to ambulatory management as outlined in Chapter 8 The dietary treatment should be supplemented *with antispasmodics and antacid medications as* well as with sedatives Althausen[6] recommends that anticholinergic medication be continued for at least 4 months and antacids for at least 6 months from the beginning of treatment It is advantageous to hospitalize the patient for a brief period

Attention should be paid to the psychosomatic aspects of the disease Peptic ulcer is a condition which develops under stressful conditions and it would appear that the prevention of recurrences in part depends on minimizing such stress in the future The necessity for active co operation on

the part of the patient cannot be overemphasized Many patients who have been labeled intractable are merely showing the result of their own failure to co operate or the failure of the physician to utilize the best plan of medical treatment

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who were followed for periods of 2 to 11 years The recurrence rate in their series for gastric ulcer treated medically without irradiation was 70 per cent and for patients receiving irradiation the recurrence rate for a comparable group of patients was only 33 per cent Patients who developed prolonged achlorhydria after irradiation had the best results recurrences occurring in only 15 per cent The recurrence rate in patients with duodenal ulcer was also decreased to approximately one half of the control value

Despite the encouraging nature of the observations following radiation therapy this mode of treatment for recurrences has not been generally adopted in the United States and other workers are less enthusiastic about its ultimate value

ANTICHOLINERGIC DRUGS It was indicated at one time that anticholinergic drugs were so effective as treatment for peptic ulcer that they could be used as the sole treatment ' and that *the continuous use of Banthine prevents the recurrence of ulcer and precludes the eventual need for surgery* " These observations were not controlled and the follow up periods were too short to justify conclusions as to the effect of the drug upon the eventual course of the disease

Subsequently a co operative long term study was undertaken to evaluate the effect of Banthine as an adjunct to conventional therapy A total of 250 patients with proved duodenal ulcers and having a known pattern of recurrences in the past were studied over a 2 year period Half of the patients were given 100 mg of Banthine four times a day while the remaining half received 0 4 mg of atropine sulfate four times a day both of these given as adjuncts to conven

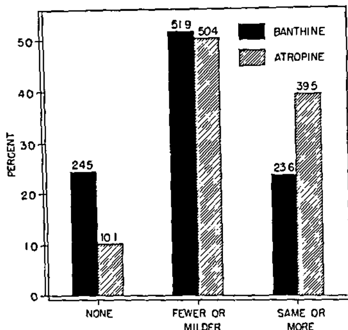


FIGURE 24

Recurrences in 250 patients treated 6 to 24 months with anticholinergic drugs (From Texter *et al* Reproduced with kind permission of the editor of the *Southern Medical Journal*)

tional treatment Of the 250 patients 131 received Banthine and 119 received atropine In the Banthine group 24 5 per cent had no recurrences while under treatment (mean period 13 months) as compared with 10 1 per cent in the atropine group (Fig 24) Both groups of patients indicated that they felt they were improved compared to their pretreatment status From the results of treatment in the mild the moderately severe and the severe cases as classified

prior to starting treatment it was apparent that the mild cases responded definitely better to Banthine than to atropine the moderate cases slightly better to Banthine and in

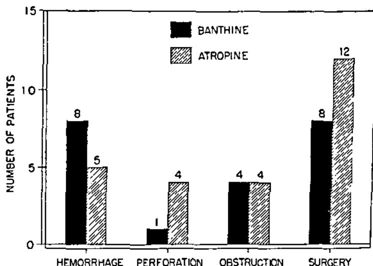


FIGURE 25

Complications in 250 patients treated 6 to 24 months with anticholinergic drugs (*From Texter et al*[1] *Reproduced with kind* permission of the editor of the *Southern Medical Journal*)

severe ulcer patients there was little difference in response to the two drugs

When objective criteria such as the incidence of complications and the necessity for surgery were studied it was noted that the incidence of complications and the necessity for surgery were the same in both groups (Fig 25) Of the 20 patients (8 per cent) who required surgery 12 had been taking atropine and 8 had been taking Banthine

It was concluded that the ulcer patients fared signifi

cantly better on conventional therapy supplemented with the anticholinergic drug Banthine than with atropine This beneficial result was inversely proportional to the estimated severity of the ulcer prior to treatment Most of the patients showed improvement compared to their pre treatment status regardless of which drug was used as adjunctive therapy Both diet and sympathetic supervision of the patient appeared to play an important role in this symptomatic improvement The improvement noted was not necessarily indicative of healing of the ulcer Persistence of ulcer craters and the failure to decrease the incidence of hemorrhages and perforations or the need for surgery indicated that the anticholinergic drug Banthine did not alter the eventual course of the disease Similar controlled clinical studies have not been carried out with all the currently available anticholinergic drugs but since the effects of the new anticholinergics now available are similar to those of Banthine it is probable that the results following their use will be similar to those observed with Banthine

General Measures of Treatment

General measures should be employed to prevent recurrences in addition to consideration of any of the specific measures mentioned above The education of the patient to an understanding of the true nature and probable course of his disease and his indoctrination into preventive measures are most important steps in preventing recurrences

EDUCATION The patient should be informed in simple terms that a specific single cause of peptic ulcer is unknown but that its recurrence is due to a constitutional predisposition to peptic ulcer working in conjunction with

prior to starting treatment, it was apparent that the mild cases responded definitely better to Banthine than to atropine the moderate cases slightly better to Banthine and in

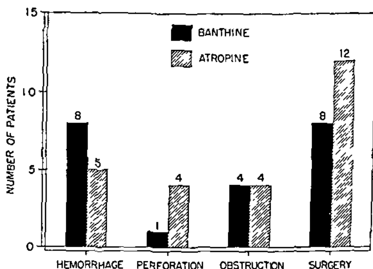


FIGURE 25

Complications in 250 patients treated 6 to 24 months with anticholinergic drugs (From Texter *et al*[1] Reproduced with kind permission of the editor of the *Southern Medical Journal*)

severe ulcer patients there was little difference in response to the two drugs

When objective criteria such as the incidence of complications and the necessity for surgery were studied it was noted that the incidence of complications and the necessity for surgery were the same in both groups (Fig 25) Of the 20 patients (8 per cent) who required surgery 12 had been taking atropine and 8 had been taking Banthine

It was concluded that the ulcer patients fared signifi

cantly better on conventional therapy supplemented with the anticholinergic drug Banthine than with atropine This beneficial result was inversely proportional to the estimated severity of the ulcer prior to treatment Most of the patients showed improvement compared to their pre treatment status regardless of which drug was used as adjunctive therapy Both diet and sympathetic supervision of the patient appeared to play an important role in this symptomatic improvement The improvement noted was not necessarily indicative of healing of the ulcer Persistence of ulcer craters and the failure to decrease the incidence of hemorrhages and perforations or the need for surgery indicated that the anticholinergic drug Banthine did not alter the eventual course of the disease Similar controlled clinical studies have not been carried out with all the currently available anticholinergic drugs but since the effects of the new anticholinergics now available are similar to those of Banthine it is probable that the results following their use will be similar to those observed with Banthine

General Measures of Treatment

General measures should be employed to prevent recurrences in addition to consideration of any of the specific measures mentioned above The education of the patient to an understanding of the true nature and probable course of his disease and his indoctrination into preventive measures are most important steps in preventing recurrences

EDUCATION The patient should be informed in simple terms that a specific single cause of peptic ulcer is unknown but that its recurrence is due to a constitutional predisposition to peptic ulcer working in conjunction with

certain unfavorable environmental factors In the majority of patients an acute ulcer will heal with medical treatment but the tendency to formation of ulcers in the future will remain so that proper preventive measures should be taken The complications which may develop including bleeding perforation or obstruction should also be pointed out

The patient should be reassured regarding the relation of ulcer to cancer Many patients have the impression that a peptic ulcer may become cancerous Since the majority of peptic ulcers are located in the duodenum one can be very emphatic in denying the possibility of cancer to these patients On the other hand because of the occurrence of malignant gastric ulcer the physician should explain to the patient with a gastric lesion the need for careful study including x ray examination gastroscopy and cytological studies when indicated It is also necessary to impress upon the patient the necessity for remaining in the hospital under strict medical management until complete healing of the gastric ulcer results or until a decision can be made whether surgical treatment should be undertaken This is discussed in Chapter 14

OCCUPATIONAL PROBLEMS Physical and mental fatigue are common causes of the recurrence of peptic ulcer In the majority of these patients the sources of emotional tension are associated with occupation The conscientious physician should be informed in regard to the nature of the patient s work his working hours his ambitions and how he spends his leisure time Modifications in such factors often can be made so that tensions are less likely to occur A change of the patient s occupation may even be necessary

Many of these occupational problems can be predicted and it seems reasonable to assume that the institution of stricter management prior to the development of symptoms will be of value in preventing recurrences

PSYCHOSOMATIC RELATIONS The typical ulcer patient has been described as a tense ambitious meticulous overly con scientious and responsible person with stoical characteris tics who tends to minimize his pain and carry on in spite of it Considerable help can be given to the ulcer patient by indicating to him the relation between his ulcer distress and his own personality Some patients neglect to take proper care of their ulcers because they feel it interferes with their work It is necessary to teach these individuals that they actually become more productive by taking care of themselves avoiding overwork taking periodic vacations and generally slowing down a little This approach to the problem is extremely valuable inasmuch as ulcer patients are frequently among our most successful business and pro fessional men making substantial contributions to society

DIET Dietary instruction is one of the important aids in preventing recurrences The importance of following a diet should be impressed upon the patient Specific instructions in regard to the diet to be followed the foods which are al lowed and the foods which are prohibited should be given to the patient (See Chapter 8)

The patient should be restricted as to the intake of drugs and foods which stimulate gastric secretion These should include coffee tea alcohol and the caffeine containing car bonated beverages Smoking also comes under this heading If these stimulants to secretion are restricted the long term results of treatment are better

INFECTIONS Ulcer recurrences frequently follow upper respiratory infections Therefore patients should be warned to guard against such infections particularly in the spring and fall seasons of the year It is desirable to treat the upper respiratory infection adequately and early so that an ulcer recurrence will be less likely to develop

PROMPT TREATMENT OF RECURRENCES The prompt treatment of recurrences is of value in minimizing the length of the recurrence and also in preventing the subsequent development of complications If prompt treatment is carried out it should be possible to prevent a considerable percentage of the episodes of epigastric distress from developing into well established ulcers

COMPLICATIONS AND THEIR RELATION TO RECURRENCES

The influence of complications of peptic ulcer is important in the future management of the ulcer patient Patients who have previously had complications are more prone to develop recurrences in the future This is illustrated by the study reported by Rae and Allison on 63 Navy men observed over a 1 year period Complications had previously occurred in 55 5 per cent of these patients During the period of the study the men lived as a corporate unit Arrangements were made for a suitable diet at regular times with snacks between meals All of the subjects in this study could have a special light diet for a few days without hospitalization if symptoms recurred At the end of 12 months more than half the men had lost time from work because of recurrent ulcer symptoms Few however had been off work

for more than a week, and it was concluded that the diet and regular living conditions were valuable in preventing incapacitating symptoms and serious relapses

Fifty two of these 63 patients were available for follow up study after 5 years had elapsed Of these 52 only 4 had no symptoms and 42 (81 per cent) had been subject to recurrent symptoms severe enough to cause them to be off work at some time Sixty two per cent of the patients lost more than 1 week of work every year and 19 per cent lost more than 3 weeks per year

The relapse rate in this group of patients was over 50 per cent during the first 12 month test period and nearly 70 per cent after 5 years Of the group that had relapsed at the end of 5 years over two-fifths of the patients had followed a fairly regular regimen of diet and alkaline powders one fifth had given up all forms of treatment, and two-fifths took alkalies and followed a suitable diet only when symptoms recurred Most of the men who had followed a fairly regular regimen were in the group in which periodic symptoms had continued Rae and Allison could not correlate the development of recurrences with dietary indiscretions defective teeth irregularity of meals or the use of tobacco and alcohol The natural course of peptic ulcer appeared to be the most important factor in determining whether the patients developed recurrences

The individual complications to be considered in relation to recurrences are persistent pain which is frequently associated with a walled-off perforation and obstruction hemorrhage and free perforation Most patients who develop repeated complications will ultimately require surgery Between 10 and 15 per cent of patients fall into this category

Pyloric Obstruction

Pyloric obstruction which is transient and can be treated by medical means does not appear to influence the frequency of recurrences If the pyloric obstruction becomes persistent the outlook for satisfactory medical management is poor and most patients in which this occurs will ultimately require surgery Gastric retention may be the result of dysfunction of the pylorus It is common in patients with pyloric channel ulcers This group of patients have either more severe recurrences or persistent symptoms and approximately 50 per cent of them require surgery

Perforation

The occurrence of perforation also influences the rate of subsequent recurrences Perforation may be the result of an acute ulcer One third of those patients who have surgical closure of a perforation will subsequently have no recurrence of their ulcers The other two thirds will continue to have recurrent distress of these approximately half will respond to medical management while the remainder will ultimately require further surgery

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and the remainder can be handled satisfactorily by medical means The specific problem of treatment of ulcer complications is discussed in Chapters 12 and 13

Persistent Pain

Persistent pain not relieved by the usual measures or having a bizarre pattern is usually indicative that some complication has developed The pain may be the result of a walled off perforation or of pyloric obstruction Persistent pain suggesting a malignancy is frequent in patients with pyloric channel ulcers In each of these instances medical treatment is not very satisfactory and the course of the patient is likely to be complicated by continued distress and more frequent recurrences than in a patient with otherwise uncomplicated ulcer [3]

Hemorrhage

Multiple hemorrhages in patients with peptic ulcer carry with them a serious prognosis Each of these hemorrhages is indicative of recurrence or continued activity of the ulcer Hemorrhage frequently occurs without prior warning of ulcer distress the onset of hematemesis or melena being the first evidence of a recurrence The majority of ulcer patients have minor bleeding episodes at intervals and 20 to 25 per cent of patients will have a major bleeding episode For some unexplained reason repeated hemorrhages tend to occur in a small group of patients as a major manifestation of their disease These patients maintain their tendency to bleed even after adequate gastric resection Wilkinson and Tracey [4] reported postresection bleeding in 33 per cent of their patients

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COMPLICATIONS AND THEIR MANAGEMENT

The exact frequency of ulcer complications is difficult to ascertain It is probable that most patients with recurrent peptic ulcer have minor bleeding episodes not serious enough to require medical attention If one limits complications of peptic ulcer to those which require specific attention and hospitalization it appears that approximately 30 per cent of ulcer patients develop such complications Most of these are the result of bleeding but free perforation into the peritoneal cavity the development of walled off perforation and the development of obstruction with resultant gastric retention are also classified as complications The majority of bleeding episodes respond readily to medical management as do some instances of pyloric obstruction The remainder of the ulcer complications usually require surgery which is necessary in approximately 10 to 15 per cent of patients with recurrent peptic ulcer

PERFORATION

Perforation which is potentially the most serious complication for the ulcer patient is fortunately rare It is prob

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PERFORATION

Perforation which is potentially the most serious complication for the ulcer patient is fortunately rare It is prob

ably not seen in more than 2 per cent of patients suffering from peptic ulceration[1] Perforation may occur at all ages from infancy to old age It is much more common in male patients A previous ulcer history can be obtained in about 60 to 75 per cent of patients with perforation and approximately 5 per cent of patients will have a history of a previous perforation Ulcers located on the anterior wall of the stomach or duodenum are most likely to perforate into the free peritoneal cavity whereas ulcers on the posterior wall of these organs are more likely to form walled off perforations bounded by adjacent structures

Clinical Features

The clinical features of perforated peptic ulcer are usually clear cut The immediate effect of perforation of the stomach or duodenum with leakage of gastric contents is a chemical peritonitis caused by the irritative gastric juices The onset of perforation is marked by a sudden excruciating pain in the mid abdomen which is usually followed by collapse The pain appears to spread throughout the entire abdomen and may radiate to both shoulders Pain radiating to the shoulders is suggestive of irritation of the undersurface of the diaphragm by either free air or gastroduodenal contents With the passage of time the chemically irritated peritoneum becomes infected and the prognosis becomes more serious

Physical examination of the patient with a perforated ulcer is characteristic The patient *lies still on his back* with the knees flexed as motion of any sort intensifies the pain The most striking physical finding is a boardlike rigidity of the abdomen with exquisite tenderness throughout The temperature in the early period *along with the blood* pres

sure may be subnormal but if bacterial peritonitis develops the temperature may become elevated

Patients who have a similar but less acute onset of symptoms may have subacute perforations There may be rigidity of the upper portion of the abdomen accompanied by nausea and vomiting The symptoms subside as the perforation becomes sealed over by adhesions

X ray examination of the abdomen is the most valuable aid in the diagnosis of perforation When possible films should be taken with the patient sitting up or lying on the left side Pneumoperitoneum is present in approximately two-thirds of patients with acute perforation

> W S a 66-year-old male had sudden onset of right upper quadrant pain with radiation to the right shoulder He had signs of peritonitis with x ray evidence of air within the abdomen (Fig 26) Laparotomy revealed perforated duodenal ulcer which was closed

Elevation of the white cell count also occurs

Differential Diagnosis

The differential diagnosis of free perforation is seldom difficult although perforated peptic ulcer may be simulated by other conditions Patients with biliary renal or small bowel colic do not have the boardlike rigidity which accompanies perforated peptic ulcer Coronary thrombosis which may resemble ulcer lacks the abdominal rigidity and the pain of coronary thrombosis frequently radiates to the left shoulder and arm The condition which is most difficult to differentiate is that of pancreatitis Boardlike rigidity is a rare finding in pancreatitis and although severe pain is present shock is less likely to occur than in perforated ulcer



FIGURE 28

\ ) lα g pne op t follo ing n te l f ll

Perforation of the gallbladder or rupture of any of the hollow viscera can simulate perforated peptic ulcer Acute cholecystitis may be difficult to differentiate from perforated ulcer although in cholecystitis the pain tends to localize in the right upper quadrant Voluntary rigidity over the gallbladder area may be present but boardlike rigidity as seen in perforated ulcer does not occur

Treatment

Closure of the perforation as soon as possible after the diagnosis is established is the treatment of choice for perforated ulcer The usual procedure consists of a simple closure of the perforation but a few surgeons have advocated gastric resection at this time The advisability of gastric resection depends upon the judgment and technical ability of the surgeon The mortality rate in gastric resection immediately following perforation is likely to be higher than when resection is performed during the interim period On occasion the surgeon has no choice but to perform a gastric resection if the perforation is so large that a satisfactory closure cannot be obtained

The mortality of perforated ulcer is low usually being below 5 per cent and it may be as low as 1 per cent It rises with increasing time after perforation and perforated gastric ulcers carry a higher mortality rate than perforated duodenal ulcers

The ultimate prognosis of the patient with a perforation has been studied by Illingworth *et al* They were able to follow 596 patients who had been operated on for perforation during a 5 year period They found that in each post operative year after the perforation approximately 2 per

cent of the patients suffered reperforation 1 per cent bled and 2 per cent found it necessary to be operated on for relief of symptoms At the end of the 5 years 30 per cent of the patients were well but 70 per cent had mild or severe recurrences of their disease It can be seen that if a large group of patients are followed after perforation approximately one third will have no further symptoms one third will have symptoms which are controlled satisfactorily by medical management while the remaining third will require further surgery [4]

There have been a few reports mainly from England of the nonoperative treatment of perforated ulcer in which constant gastric suction and concurrent antibiotics are used Good results have been reported following this form of therapy but it is felt that nonoperative treatment should be limited strictly to those cases of perforation of many hours duration or to instances where surgical closure cannot be undertaken Excellent bedside care is essential for these patients and their recovery is considerably slower than when surgical closure of the perforation is carried out Even the enthusiastic supporters of this mode of treatment indicate that increasing rigidity and tenderness are indications for operative intervention Not enough patients have been treated in this manner to evaluate the mortality rate in nonoperative treatment as compared with the rate following surgical closure

WALLED-OFF PERFORATION

Walled off perforation results when the process of perforation involves ulcers located on the posterior wall of

either the stomach or duodenum These ulcers rarely perforate into the free peritoneal cavity but penetrate to involve the entire thickness of the stomach and duodenum and adjacent structures An inflammatory mass is present usually without abscess formation

The incidence of walled off perforation is difficult to estimate The diagnosis is seldom made by x ray examination and autopsy statistics are of little value in establishing its incidence The only source of material is that provided by the surgeon Even at surgery it may be difficult to be certain whether the ulcer has perforated and walled off to involve adjacent structures Inasmuch as only 10 to 15 per cent of ulcer patients are treated surgically it is apparent that the surgeon cannot give a true picture of the incidence of walled off perforation It appears likely that most patients whose ulcers have become refractory to the usual medical care have a walled off perforated ulcer Walled off perforation is at least as common as free perforation probably even commoner Ruffin estimates that 5 per cent of all ulcer patients at one time or another develop this complication

Clinical Features

The clinical features presented by the patient with a walled off perforated ulcer have been studied The organs most frequently involved in this process are the pancreas and the liver In a series of 100 cases reported by Cassel *et al* the pancreas was involved in 76 patients the liver in 9 and an inflammatory mass adjacent to the liver was present in an additional 8 patients

Certain features are suggestive of the development of a walled off perforation These consist of either a change in

the usual pain pattern the development of increasingly severe ulcer pain or the radiation of pain to the back One or more of these features were present in 71 per cent of the patients studied [1] This change in pattern is not necessarily diagnostic of a perforated walled off gastroduodenal ulcer as a change in the clinical pattern may be found in other conditions including pyloric obstruction and ulcers located in the pyloric channel [7]

Physical findings are not very helpful in making the diagnosis of perforated walled off ulcer Most of these ulcers are located on the posterior wall of either the stomach or duodenum and the physical findings do not differ from those in uncomplicated gastric or duodenal ulcer

Laboratory findings are of little value in establishing the diagnosis The white cell count is usually normal unless an abscess develops An elevation of the serum amylase may be present as a result of a localized pancreatitis [8] The elevation of the serum amylase is of moderate degree and can be distinguished from that due to acute pancreatitis in that it is not greater than five times the normal values as frequently occurs with acute pancreatitis The results of gastric analysis and examination of the stools for occult blood do not differ from those of patients with uncomplicated ulcer

The roentgenologist can occasionally suspect the presence of penetration and walled off perforation especially in gastric ulcers There may be a pouch with a narrow neck or a fluid level within the pouch Pockets of air can be demonstrated projecting from the stomach and these are thought to indicate perforation The roentgenologist is of little help in establishing the diagnosis of perforated walled off ulcer involving the duodenum as the x ray signs of posterior pene

tration and perforation do not differ from those ordinarily present with duodenal ulcer If an ulcer is located in the gastroscopically visible area of the stomach it can be demonstrated gastroscopically but it is usually not possible to determine whether the base of the ulcer consists of the stomach or an adjacent organ

Differential Diagnosis

The differential diagnosis of perforated walled-off gastroduodenal ulcer presents problems for the physician The history differs from that obtained in the usual ulcer case and frequently the patient is unaware that his distress is arising from an ulcer The diagnosis may be made by the orthopedic surgeon or neurologist because originally the patients were thought to have an orthopedic or neurologic problem

Walled off perforated ulcer may be difficult to differentiate from pancreatic disease Since the pancreas is the organ most frequently involved in the development of a walled off perforation localized pancreatitis is frequently present The pain which results may be identical to that of primary pancreatitis Elevation of the serum amylase may occur in both conditions but an elevation of more than 500 mg or more than five times the normal value is definitely suggestive of primary pancreatitis rather than a walled off perforation Pancreatic calcification steatorrhea and diabetes are all indicative of a primary pancreatic process Carcinoma of the pancreas may simulate walled off perforation

Walled-off perforated ulcer must also be differentiated from biliary tract disease carcinoma of the stomach and diseases of the spine Whenever a reasonable doubt exists as to the real nature of the condition and exploratory lapa



FIGURE 27
X ray showing a penetrating duodenal ulcer

rotomy should be performed Some of these problems are illustrated by the following case

E F a 47 year old white male had a 10 year history of duodenal ulcer He developed left sided constant pain not relieved by food or alkali and anorexia and vomiting after years of typical ulcer symptoms X ray showed a posterior penetrating duodenal ulcer (Fig 27) Resection was required

TREATMENT

Intensive treatment in the hospital is indicated for all patients suspected of having a walled off perforated gastric or duodenal ulcer The anticholinergic drugs either oral or

parenteral may be of considerable help The parenteral preparation can be given either by intramuscular injection every 6 hours over a period of several days or by intra muscular injection each time the ulcer distress recurs The latter method is preferable as it enables the physician to evaluate the symptomatic improvement of the patient [9]

Constant gastric suction during the night is valuable An indwelling stomach tube may be used and a milk or antacid drip employed to control the secretion of hydrochloric acid during the night The initial response to treatment may be satisfactory in terms of symptomatic relief but recurrences are more likely to occur than in patients with uncomplicated ulcers Many of these patients are refractory to even the most rigid medical program and surgical treatment becomes necessary A period of intensive medical management in the hospital is indicated in all patients however before con sidering surgery

Surgical treatment ultimately becomes necessary for some of these patients who do not respond to intensive medical management The decision whether surgery is necessary and just when it should be performed is a difficult one The only indication for surgery frequently is that of intractability If constitutional symptoms are present suggesting abscess for mation surgical drainage may be necessary prior to resec tion The surgical aspects of this problem are considered in Chapter 13

HEMORRHAGE

Hemorrhage is the most frequent complication affecting the ulcer patient Many patients with active ulcers have

minor bleeding episodes but do not recognize them and as a result they do not come to the attention of the physician Approximately 20 to 25 per cent of patients with ulcer experience fairly massive bleeding requiring medical attention Ulcers located on the posterior wall of the duodenum are the ones most prone to bleed Most hemorrhages are mild and the over all prognosis is good but fatal exsanguinating hemorrhages do occur Fatal hemorrhages are almost always arterial in origin and a branch of one of the major arteries may be seen protruding from the base of the ulcer Arteriosclerosis which prevents the vessel from retracting in the usual manner is usually present

Clinical Features

Hemorrhage from the upper gastrointestinal tract may be manifested by the passage of tarry stools or if the hemorrhage is more severe by the vomiting of bloody or coffee ground material If the hemorrhage is small or occult it may go unnoticed by the patient At other times the symptoms may be only those of blood loss with either the sudden development of weakness or the feeling of fatigue or faintness associated with chronic blood loss Ulcer pain which may have been previously present frequently disappears with the onset of a severe hemorrhage Perhaps this is related to Illingworth s concept that engorgement of the gastric or duodenal mucosa is important for the development of pain (See Chapter 5)

Pallor may be noted on physical examination and if the bleeding is brisk enough one may have evidence of hemorrhagic shock If more than 30 per cent of the circulating blood volume is lost irreversible hemorrhagic shock occurs

Endoscopy is rarely performed while the patient is actively bleeding but occasionally it is necessary to do so particularly if a differential diagnosis must be made between bleeding from esophageal varices and bleeding from an ulcer The bleeding point may be demonstrated This is especially valuable if the x ray examination of the upper gastrointestinal tract is negative

X ray examination is delayed until the patient has ceased to bleed However if the bleeding is brisk and surgery is considered x ray examination may be carried out shortly after the onset of hemorrhage the Hampton technique[10] being employed In this approach the barium is administered to the patient without the use of compression blocks or manual palpation Zamcheck *et al*[1] have reported on the accuracy of early x ray diagnosis of massive gastrointestinal hemorrhage X ray studies were carried out for 123 patients 74 of whom were examined within the first 48 hours after admission Complete examinations including the use of pressure cones were performed for 43 patients The initial x ray diagnosis was confirmed in 92 of the 123 patients It was concluded that emergency x ray examination of the gastrointestinal tract could be performed with reliability and with greater safety to the patient than had been believed possible formerly If the diagnosis is not clear on the initial examination the x ray studies should be repeated

Differential Diagnosis

Hemorrhage originating from peptic ulcer accounts for most instances of massive gastrointestinal bleeding but it still must be differentiated from other causes of hematemesis or melena Bleeding into the gastrointestinal tract may oc

minor bleeding episodes but do not recognize them and as a result they do not come to the attention of the physician Approximately 20 to 25 per cent of patients with ulcer experience fairly massive bleeding requiring medical attention Ulcers located on the posterior wall of the duodenum are the ones most prone to bleed Most hemorrhages are mild and the over all prognosis is good but fatal exsanguinating hemorrhages do occur Fatal hemorrhages are almost always arterial in origin and a branch of one of the major arteries may be seen protruding from the base of the ulcer Arteriosclerosis which prevents the vessel from retracting in the usual manner is usually present

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the rule and vigorous treatment may be necessary As a result of continuous bleeding changes in the circulatory system may take place resulting in shock which ultimately becomes irreversible There is a fall in blood pressure and a loss of circulating blood volume This can produce anoxemia in vital organs especially the heart brain and kidneys The prolonged shock which results from hemorrhage may result in azotemia which further complicates treatment Loss of 30 per cent or more of total blood volume from hemorrhage will produce death unless transfusions are given [23]

The usual medical treatment of bleeding ulcer prior to 1931 consisted of bed rest starvation the use of morphine and an icebag to the epigastrium After 3 or 4 days of starvation treatment the patient was started on a modified type of Sippy diet The results of this treatment were not very satisfactory and in a large group of cases collected by Miller and Elsom [4] the mortality rate was 8 7 per cent

The widespread use of the prompt feeding program of the bleeding ulcer patient was initiated by Meulengracht [15, 16] in 1931 although Andreson had proposed it earlier Meulengracht had observed that patients with hemorrhage frequently stopped bleeding when they were given food and that ambulatory patients would recover from melena without any change in their diet He pointed out that the empty stomach was more active than the full stomach and that the combination of an empty stomach with the presence of unneutralized free hydrochloric acid was poor treatment for peptic ulcer Meulengracht began feeding patients with a bland diet of 5 meals a day and in 1947 summarized the results of this form of treatment in 1031 consecutive bleeding ulcer patients [7] The mortality rate was 2 5 per cent and if

cur with the blood dyscrasias including leukemia hemolytic icterus purpura splenic anemia and hemophilia The most common cause of gastrointestinal hemorrhage simulating that originating from peptic ulcer is carcinoma or esophageal varices These two lesions can usually be distinguished by x ray examination although at times they present problems in differential diagnosis The Bromsulphalein test is valuable in distinguishing between bleeding having its origin in esophageal varices and bleeding arising from peptic ulcer[1] The Bromsulphalein may be elevated temporarily during the period of bleeding in patients with peptic ulcer but repeated tests demonstrate that it falls rapidly to normal in the absence of liver disease The use of the Bromsulphalein test along with the clinical features x ray study and endoscopic examination should be of assistance in excluding esophageal varices when emergency surgery is contemplated in massive gastrointestinal hemorrhage Bleeding may also result from hiatus hernia or gastritis but it is seldom so severe as to require emergency surgical treatment

TREATMENT

The treatment of hemorrhage from gastroduodenal ulcer varies according to the severity and nature of the bleeding Bleeding is commonly the result of vascular granulation tissue at the base of the ulcer or an erosion of a small vessel in an area surrounding the ulcer In the majority of such cases bleeding will cease spontaneously as a result of normal physiologic mechanisms If the bleeding arises from a major arterial vessel or if there is significant arteriosclerosis present continuing or recurrent hemorrhage will result Spontaneous cessation of the bleeding in this situation is not

gastrointestinal tract the blood urea nitrogen will rise This falls as the bleeding ceases and less absorption takes place The blood urea nitrogen is of value in following the progress of the hemorrhage Another index of the degree of bleeding is the number of stools passed daily Blood acts as an irritant within the bowel with the result that frequent copious tarry stools are passed

If the bleeding is brisk and there are signs of shock an infusion should be started while whole blood is being obtained and the hematocrit should be checked to make sure that the blood volume is being maintained If the blood volume decreases in spite of the administration of blood it indicates that the hemorrhage is proceeding at a rate faster than the blood is being replaced

Dietary treatment should be started as soon as the patient is able to eat Some physicians prefer to treat the bleeding ulcer patient initially with the first stage diet and antacids while others prefer to use the Meulengracht type of diet This diet is a bland one including ground meat with concurrent antacid therapy as outlined in Chapter 8 Those who prefer the use of meat feel that there may be something in the meat itself which aids in the formation of a blood clot and assists *in stopping the bleeding The use of a diet* containing meat presents problems in the evaluation of whether the patient has ceased bleeding or not One can have false positive values for occult blood in the stool if the benzidine reagent is used Some of the newer modifications of the occult blood test may be of value in this situation The quantitative evaluation of gastrointestinal bleeding using radiochromium labeled erythrocytes may ultimately be of clinical value too Experimental studies have indicated that the

patients were excluded who died from other causes as well as those who died within the first 24 hours it was 1 5 per cent

These statistics have been criticized because many cases of mild ulcer in which bleeding would have ceased spontaneously were included in this series and the diagnosis of ulcer was not proved in all of the patients In response to this criticism Meulengracht compared his results with those of Christiansen[18] who employed the starvation method of treatment under similar circumstances at approximately the same time in Denmark The mortality rate of Christiansen s patients was 7 9 per cent

The results of the prompt feeding program in this country were also gratifying Rasberry and Miller[3] for a collected series of 2111 patients reported a mortality rate of 4 per cent which was reduced to 1 9 per cent when patients were excluded who were moribund on admission or died from other causes Even though the Meulengracht plan of management has been modified most authorities agree that prompt feeding as soon as the patient is able to eat is a more physiologic approach to treating the bleeding ulcer patient than the old starvation routine and that it is accompanied by a lower mortality rate

The bleeding patient should be advised to enter the hospital immediately He is put to bed and checked for shock The blood pressure and pulse should be recorded at hourly intervals and the blood should be typed and cross matched in the event that transfusion becomes necessary A blood count hemoglobin or hematocrit should be done on admission to the hospital and repeated at frequent intervals thereafter If a significant amount of blood has been lost into the

48 to 72 hours The surgeons also point out that there are dangers inherent in p olonged blood administration includ ing the possibility of transfusion reactions and the subsequent development of serum hepatitis In spite of these dangers the results of the average medical program are statistically superior to the results of the average surgical therapy for a hemorrhagic ulcer

The best results in treating the bleeding ulcer patient are obtained when medical and surgical departments act as a team In most hospitals the bleeding ulcer patient is admitted to the medical service with the surgeon being called in consultation whenever there is a possibility that surgery may be necessary The surgeon therefore becomes a partner in supervising the patient during treatment and any decisions as to the subsequent treatment of the bleeding become a joint responsibility

The decision as to what type of surgery to perform may be a problem The surgeon may be unable to localize the bleeding point even after inspecting the interior of the stomach and duodenum If the diagnosis of ulcer was established prior to initiating surgical treatment a partial gastrectomy either with or without vagotomy should be performed The problem of elective surgery after recovery from an acute hemorrhage is discussed in Chapter 13

OBSTRUCTION

Gastric retention due to transient obstruction of the distal portion of the stomach is a common complication of ulcer If the retention is due to edema or spasm of the pylorus it usually responds to medical management but if the changes

amount of blood entering the intestine could be evaluated with fair precision down to a volume of 5 ml or less [9]

The antisecretory drugs including belladonna atropine and the newer anticholinergic agents, have all been employed as adjunct treatment for the bleeding patient The usefulness of the newer anticholinergic drugs in this situation seems questionable and some evidence that they may be actually contraindicated is present [9]

The use of a milk or antacid drip therapy has been advocated in the treatment of bleeding peptic ulcer The intragastric administration of gel foam along with topical thrombin also has been reported to improve the results of medical treatment as compared with the conventional medical management

The majority of bleeding ulcer patients respond to medical treatment Surgery may be necessary especially in patients over 45 years of age who have had either recurrent or prolonged hemorrhages It is hazardous to attempt surgery if the diagnosis is in doubt and it is recommended that x ray examination be carried out prior to surgery to rule out other causes for the bleeding such as esophageal varices or cancer This can be safely performed with little risk of promoting further bleeding [11] Esophagoscopy or gastroscopy occasionally is necessary in order to establish the correct diagnosis

The mortality rate in surgical treatment for bleeding is higher than in medical treatment Miller and Elsom [14] reported a mortality rate of 28 per cent in 383 cases of massive hemorrhage which were treated surgically The mortality rate has decreased in recent years and it has been emphasized by surgeons that an early operation carries a lower mortality rate than when operation is delayed for more than

48 to 72 hours The surgeons also point out that there are dangers inherent in prolonged blood administration including the possibility of transfusion reactions and the subsequent development of serum hepatitis In spite of these dangers the results of the average medical program are statistically superior to the results of the average surgical therapy for a hemorrhagic ulcer

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better with something in the stomach Weight loss and signs of dehydration are late features of the obstructing ulcer

Signs of weight loss may be evident on examination Succussion splash and the outline of an enlarged distended stomach can sometimes be observed Visible peristalsis which passes from the left to the right is characteristic of pyloric obstruction

Roentgenologic study of the stomach is useful in evaluation of the degree of pyloric obstruction The stomach normally empties within 6 hours after administration of the usual barium mixture If significant retention is present barium is retained longer than 6 hours and sometimes for as long as 24 hours Retained food and secretion can be observed within the barium mixture The stomach may empty normally as measured by the usual barium meal technique and the patient still have difficulty eating a normal meal A barium food mixture can be used to simulate the usual meal to determine if gastric retention is present under these circumstances

Gastric aspiration is of value in determining the degree of gastric retention The fasting stomach does not contain more than 75 to 100 ml in the morning specimen normally nor secrete more than 750 ml during the 12 hour overnight period of continuous suction Values for overnight secretion in excess of 750 to 1000 ml are indicative of hypersecretion pyloric obstruction or both

Differential Diagnosis

Organic pyloric stenosis secondary to ulcer must be differentiated from pyloric stenosis from other causes Disorders

are of long duration significant pyloric stenosis may be present One may also have reflex delays in gastric emptying especially in patients who have gastric ulcers located on the lesser curvature below the angularis or in patients who have pyloric channel ulcers [7]

Changes in both the motor and secretory activities of the stomach occur as a result of obstruction at the pylorus Gastric motility increases and ultimately the stomach becomes dilated Hypersecretion with high acidity and an increase in secretory volume also occurs in patients with pyloric stenosis

Clinical Features

The clinical features of pyloric obstruction initially are not diagnostic and the diagnosis is frequently made following x ray examination or aspiration of the stomach Changes in the character of the ulcer distress may be observed as the process becomes more severe The pain has less relation to meals and is not readily relieved by the ingestion of food or alkali Breakfast is the best tolerated meal of the day subsequent meals may be followed by nausea and fullness Vomiting may occur especially in the early hours of the day The vomitus contains food remaining from the previous meal and sometimes even longer

The changes in the characteristics of the pain are helpful in establishing the diagnosis of obstruction The pain of obstructing ulcer may become less severe but more constant Patients with obstructing ulcers frequently describe a sensation which is related to distention of the stomach this can be relieved by vomiting They indicate that they feel better on an empty stomach whereas previously they had felt

the presence of obvious pyloric stenosis They have been used when it was thought that obstruction was due to edema rather than to stenosis but even in this situation their value would seem to be questionable

A simpler method, which we prefer for handling pyloric obstruction is to aspirate the stomach initially and leave the tube in place during the 12 hour overnight period continuous gastric suction being employed. The tube can then be removed during the day and the patient fed at hourly intervals a liquid diet of milk and cream and antacids Electrolyte disturbances are less likely to occur when this approach is utilized than when continuous aspiration is carried out. This method also has the advantage of providing an index of the progress of treatment The amount of gastric aspirate obtained each night during the 12 hour period can be measured, and if this amount shows a gradual decrease during treatment, progress is being made towards restoring normal gastric evacuation.

X ray study of the stomach is useful in determining whether medical treatment is progressing satisfactorily These studies should be repeated at intervals of 5 to 7 days If improvement takes place both in the roentgenologic appearance of the stomach and the amount of aspirate obtained the diet can be liberalized so that by the time of discharge from the hospital the patient is on an ambulatory type of program

Surgical treatment must be considered, after correction of the nutritional problem, in patients who do not respond to medical management. In the past it was thought that gastroenterostomy was sufficient surgical treatment for the obstructed ulcer patient. It is now recommended that these pa

of gastric motor function due to extragastric conditions should be considered Other disorders involving the stomach can also produce gastric retention An obstructing carcinoma of the distal stomach is the one which frequently presents the most difficulty Hypertrophic pyloric stenosis congenital or acquired can produce a similar x ray picture Gastric retention is a frequent roentgenologic finding in patients with benign ulcers located within the channel area Obstruction of the second portion of the duodenum as a result of the superior mesenteric artery syndrome may also produce delay in gastric evacuation This condition may be suspected clinically if the vomitus contains bile suggesting that the obstruction is distal to the ampulla of Vater

TREATMENT

The treatment of pyloric obstruction requires hospitalization A decision must be made whether the patient can be managed medically or should be treated surgically The medical treatment of pyloric obstruction with gastric retention consists of aspiration of the stomach in conjunction with a liquid diet antacids and antispasmodics Aspiration serves to restore tone so that the motor functions of the stomach become more normal and it aids in decreasing edema in the area of the outlet of the stomach Aspiration can be carried out continuously but careful record must be made of the amount of gastric aspirate obtained so that electrolyte balance can be maintained by the administration of parenteral fluids The gastric tube can be clamped at intervals after initiating feedings of milk and cream

The newer anticholinergic agents are contraindicated in

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15 MEULENGRACHT E. *Lancet* 2 1220 1935
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tients be treated like other patients with active ulcer either by gastric resection with or without vagotomy or by gastroenterostomy with vagotomy

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century. Modifications were made in the technique of gastric resection and gastroenterostomy; the most commonly used operations are represented diagrammatically in Figure 28.

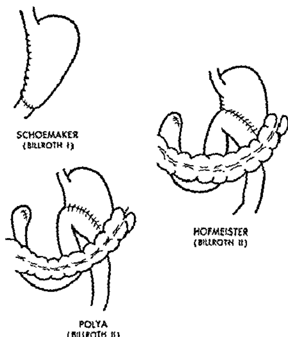


FIGURE 28

Diagrammatic representation of commonly employed types of gastric resection.

Gastroenterostomy was the operation most frequently performed in the earlier years until 1925, when Lewisohn reported on a 2-year follow-up of the operations of gastroenterostomy, ulcer excision, cautery puncture and pyloroplasty. Only 50 per cent of the patients were cured and at

13

SURGICAL TREATMENT

Surgical treatment for peptic ulcer had its beginnings in the nineteenth century with the performance of the first successful gastrojejunostomy by Wolfler in 1881 [1] The first successful partial gastrectomy was performed earlier in the same year by Billroth to remove a gastric cancer A partial gastric resection was first employed by Rydygier in 1882 for the treatment of an inflammatory pyloric ulcer This was followed in 1886 by the independent use of pyloroplasty by Heincke and Mikulicz [1]

DEVELOPMENT OF SURGERY

Following the introduction of the operations of gastric resection gastroenterostomy and pyloroplasty within a five year period interest in the surgical treatment of peptic ulcer waned After it was shown that the roentgenologic technique could be used to demonstrate the gastrointestinal tract surgeons again became interested in the treatment of peptic ulcer *Rapid strides were made in the development of surgical techniques* during the first two decades of the twentieth

cedure preserves the antrum but removes 85 per cent of the acid secreting area Berne[8] has combined vagotomy pyloroplasty and a large resection of the body of the stomach The ulcer is left in place gastroduodenal continuity is preserved and the effects of vagotomy and pyloroplasty are obtained

INDICATIONS FOR SURGERY

Surgical treatment is necessary for between 10 and 15 per cent of patients with chronic or recurrent peptic ulcers This surgery may be of two types either emergency surgery necessary to save the life of the patient whose ulcer has perforated or who has uncontrolled gastrointestinal hemorrhage or elective surgery in which the aim is to prolong life and render the patient free of disabling symptoms

Surgical intervention should be limited to patients who develop complications or who have not responded to treatment despite adequate medical management[1] The indications for surgical treatment are (1) perforation (2) obstruction (3) hemorrhage (4) intractability or failure of medical management (5) suspicion of carcinoma and (6) complications secondary to previous surgery

Perforation

Surgical closure of the perforation as soon as possible after the diagnosis is established is the recommended treatment although a few surgeons have advocated gastric resection at this time Unless exceptional conditions prevail more definitive gastric surgery should be deferred until a later date (See Chapter 12)

least 30 per cent developed new ulcers at the stoma margin or had recurrent ulcers at the site of the old lesions Many of the patients were worse off following surgery than they had been before operation [1]

With this demonstration of the unfavorable late results of simple gastroenterostomy the surgical procedure of gastric resection was revived Increasingly larger portions of the stomach were removed until a 65 to 75 per cent resection was considered the operation of choice This operation was completed by a short loop gastroenterostomy The acid stimulating mechanism of the antrum was thereby removed

Dragstedt in 1945 reported his experience with the operation of vagotomy Although this procedure was not new having been tried before and abandoned Dragstedts experimental work indicating that it abolished the cephalic phase of gastric secretion established its rationale on a sound physiologic basis The results following vagotomy alone were unsatisfactory and subsequently the operation has been combined with gastrojejunostomy or pyloroplasty

Dissatisfaction with the several operations has led to recent effort to find a more satisfactory surgical treatment for duodenal ulcer Vagotomy has been combined with partial gastrectomy the latter varying from 50 to 75 per cent The Billroth I gastric resection has been revived in a desire to minimize the side effects of the Billroth II type of gastrojejunostomy particularly the dumping syndrome and nutritional deficiency Moore and Harkins have reported on an extensive series of cases of duodenal ulcer treated in this manner Another approach to the problem of preserving gastroduodenal continuity is that of Wangensteen [8] who performs a segmental resection of the stomach This pro

bleeding episode Continuous massive hemorrhage in patients over 55 years of age usually requires surgical treatment The mortality rate for gastric resection when the patient is actively bleeding is higher than when surgery is carried out in the interim phase

Review of the patient's history is helpful in deciding whether surgery is to be performed in the patient with bleeding ulcer Patients with penetrating ulcers tend to have a more unrelenting type of hemorrhage than those without evidence of penetration The majority of patients who require surgical treatment for their hemorrhages have either a history of intractable pain preceding the hemorrhage a history of past bleeding or a history of a previous perforation [1]

Subtotal gastric resection is the operation usually performed but vagotomy in conjunction with gastric resection appears to be valuable in surgical treatment of the bleeding ulcer patient Direct ligation of the vessels in the area of the ulcer as treatment for bleeding has not been successful

INTRACTABILITY OR FAILURE OF MEDICAL MANAGEMENT

Intractability is the most ill defined of the indications for surgery in peptic ulcer Intractability means different things to different people and tends to be relative Patients who have severe ulcers with considerable inflammation and the development of a walled-off perforation do not respond well to medical treatment and surgery is usually necessary for them A less severe degree of medical failure is the case in which the patient responds to medical management while in the hospital but has a prompt recurrence shortly after discharge from the hospital The decision as to the future

The expectant suction method of conservative approach to perforation has been advocated Although good results have been claimed with this method it appears that the best over all results are achieved by adhering to the time honored procedure of direct plication closure of the perforation by surgical means

Obstruction

Pyloric obstruction if it is persistent and a result of scarring requires surgical treatment The type and degree of benign obstruction can be determined by periodic gastric aspirations X ray examination of the stomach is also useful in determining the degree of gastric retention More than 50 per cent gastric retention in 6 hours or any gastric retention at 24 hours is usually indicative of organic stenosis

The initial treatment regardless of whether surgery will ultimately be indicated is medical If the retention does not respond to conservative treatment by suction and a liquid diet electrolyte and nutritional disturbances should be corrected as far as possible and surgery carried out

Hemorrhage

The majority of patients with gastrointestinal hemorrhage will respond to medical management but surgical treatment is necessary if the bleeding is prolonged or recurrent It may be difficult to decide when surgical treatment is indicated for patients with bleeding ulcer Many factors enter into making a decision including the patient s age his general condition the number of previous bleeding episodes and his past response to medical management Surgery should be considered if the patient has had more than one massive

nant and in those patients who developed recurrence 16 per cent of the ulcers were malignant The differentiation of a benign from a malignant gastric ulcer presents many problems The problem of the gastric ulcer and its relation to carcinoma is discussed in detail in Chapter 14

Complications Secondary to Previous Surgery

Marginal or recurrent ulcer which follows a previous gastroenterostomy or gastric resection may require further surgery On occasion it is necessary to operate in order to revise previous surgery in an attempt to eliminate severe postsurgical disability Both of these problems are taken up in the section on postgastrectomy syndromes

CHOICE OF OPERATION

The first operation that was widely adopted in the treatment of peptic ulcer was gastroenterostomy The immediate results of treatment were good but the ultimate results were not so satisfactory Lewisohn [1] reported in 1925 that the incidence of gastrojejunal ulcers in patients who had been treated with gastroenterostomy was 34 per cent and urged that surgeons be more radical in their surgical treatment of duodenal ulcer Gradually increasing resections of the Billroth II type were performed during the succeeding twenty years and by 1945 it was agreed that two-thirds to three quarters of the stomach should be removed to achieve a satisfactory postoperative result

About the same time that gastric resection became established as a treatment of choice for both gastric and duodenal ulcer Dragstedt and Schafer proposed the use of vagot

management of such patients depends upon the severity of the recurrences and the degree of disability Economic factors must frequently be considered

The degree of pain present may be useful as a guide When ulcer pain becomes so severe or so incapacitating to *the patient that he no longer feels able to carry on his usual* activities the results of surgery are usually good It should be emphasized to such patients before surgery that dietary restrictions will be necessary after surgery and that there is always the possibility of their developing some complications or a recurrent ulcer Between 10 and 15 per cent of patients operated upon have unsatisfactory results The mortality rate accounts for 3 to 6 per cent of these individuals while between 4 and 9 per cent have recurrences or complications following their surgery

Continuation of medical treatment after the development of complications however is not without danger Moore *et al* reported on 997 patients 738 of whom had duodenal ulcer which was managed entirely by medical therapy These patients were followed for 2 to 8 years The mortality rate was 2 03 per cent in those patients managed medically This mortality rate was entirely attributable to ulcer complications

Suspicion of Cancer

The mere presence of a gastric ulcer which may be malignant is used by some as an indication for surgery This is based on the observation that a certain number of gastric cancers masquerade as gastric ulcers In a series of 1000 gastric ulcer patients Smith *et al* after excluding obvious malignancies found 8 8 per cent of the ulcers to be malig

nant and in those patients who developed recurrences 16 per cent of the ulcers were malignant The differentiation of a benign from a malignant gastric ulcer presents many prob lems The problem of the gastric ulcer and its relation to carcinoma is discussed in detail in Chapter 14

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omy for the treatment of duodenal ulcer At the present time vagotomy is seldom used as a sole operation but is combined with partial resection gastroenterostomy or pyloroplasty

Gastroduodenostomy commonly referred to as the Billroth I operation is also being revived for the treatment of duodenal ulcer It had been used for gastric ulcer but largely discarded for the treatment of duodenal ulcer Moore and Harkins have comprehensively reviewed this subject in an attempt to re evaluate the usefulness of the Billroth I operation in the surgical treatment of peptic ulcer both gastric and duodenal Another development along similar lines is the revival of the tubular resection operation by Wangensteen [9] This operation also maintains continuity of the stomach and duodenal area and like the Billroth I operation is thought to have fewer postoperative complications

RESULTS OF SURGERY

The results of surgical treatment of peptic ulcer are extremely difficult to evaluate Any rational evaluation must take *into account the type of operation employed the* mortality rate the early and late results of treatment and the incidence of complications The results can be classified on the basis of the location of the ulcer

Esophageal Ulcer

Surgical treatment is rarely indicated in esophageal ulcer However massive hemorrhage perforation or intractability to medical management may require surgery The procedures employed include correction of concurrent hiatus her

nia partial resection of the esophagus subtotal gastrectomy and vagotomy and gastroenterostomy The results are only fairly good

Gastric Ulcer

Surgical treatment of gastric ulcer is generally very satisfactory Marginal ulcer is extremely rare following gastric resection for a gastric ulcer The major problem in gastric ulcer is deciding when surgery should be carried out and distinguishing patients with malignant ulceration from those with benign ulcer The latter problem is taken up in Chapter 14

Duodenal Ulcer

There is considerable controversy regarding surgical treatment in duodenal ulcer This controversy concerns the type of surgery to be carried out and in particular what place vagotomy has A preliminary evaluation can be made but the ultimate evaluation of the merits of vagotomy with gastroenterostomy versus those of subtotal resection must await further clinical trial with long follow up periods [1]

After resection of two thirds to three quarters of the stomach about 85 per cent of patients will have satisfactory results Recurrent ulceration at the junction of the stomach and jejunum will develop in 4 to 8 per cent of patients after surgery while an additional number may have postoperative complications Moore and Harkins have tabulated the hospital mortality rates for a series of reports in the literature from 1947 to 1953 observing a range of values from 0 to 27 per cent The average rate was between 3 and 5 per cent The complications which follow gastric resection include recurrent or persistent ulceration the dumping syndrome

symptoms due to alterations in carbohydrate metabolism anemia and postoperative weight problems

The results of treatment following vagus nerve section are more difficult to evaluate as the operation is still under judgment Transthoracic vagotomy without a drainage operation was recommended initially but the results were not satisfactory and the operation of vagotomy alone has been abandoned It is now combined with either gastroenterostomy gastric resection or pyloroplasty

The National Committee on Peptic Ulcer of the American Gastroenterological Association has reported on a comparative study of vagotomy and gastric resection [15] The Committee under the chairmanship of Sara Jordan studied the results of vagotomy alone vagotomy combined with gastroenterostomy and vagotomy combined with partial gastric resection The results of treatment with gastric resection were evaluated when less then 70 per cent of the stomach was removed and when more than 70 per cent was removed Vagotomy was evaluated in 4076 cases of peptic ulcer treated with vagotomy alone or in combination with other surgical procedures The results of partial gastric resection were evaluated in 1163 patients Insofar as possible the same surgeons in the same hospital centers co operated in the two surveys When these two groups of patients were compared there was no difference in the satisfaction with the surgery as classified subjectively in patients having gastric resection and those having vagotomy with gastroenterostomy A satisfactory result was reported by 94 per cent of the patients *in both groups The mortality rate was 2 5 per cent for the* resected patients who had not bled previously while the mortality rate for the vagotomy and gastroenterostomy pa

tients who had not bled previously was 1 4 per cent The mortality rate for patients who had not bled previously in the gastric resection group was 5 4 per cent which compared with 1 per cent in the vagotomy and gastroenterostomy group Despite the higher mortality rate following gastric resection the Committee concluded that the results of treatment by gastric resection would appear to be slightly better than those of treatment by vagotomy with gastroenterostomy This advantage of gastric resection over vagotomy with gastroenterostomy for duodenal ulcer was shown only if an estimated 70 per cent or more of the stomach was removed

Grimson[16] on the basis of a critical study of the report of the Committee came to the conclusion that in view of the lesser mortality risk and the comparatively favorable results vagotomy with gastrojejunostomy was the preferable procedure These observations were supported by the results of his own studies of vagotomy with gastroenterostomy in 135 patients as compared with the results of subtotal gastric resection in 132 patients[17, 18]

Pollard *et al*[9] have compared the results of vagotomy with gastroenterostomy and subtotal gastrectomy for duodenal ulcer in a series of cases all done within the same year and followed for 5 years Satisfactory results were obtained in 85 7 per cent of the 38 patients in the vagotomy with gastroenterostomy group Recurrences were observed in 4 7 per cent There were no operative deaths In comparison 86 8 per cent of the 53 patients having subtotal gastric resection had satisfactory results recurrences occurred in 9 4 per cent There was a 6 per cent operative mortality for the gastric resection group They concluded that satisfactory results or

symptoms due to alterations in carbohydrate metabolism anemia and postoperative weight problems

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erably in the numerous reports in the literature. Glenn and Harrison [3] report a mortality rate of 1.9 per cent, with 87 per cent of their patients having satisfactory results following operation. Eastman and Cole [4] report a mortality rate of 5.8 per cent, while others report rates of 2.86 per cent [12] and 5.8 per cent [1].

The next most serious complication of gastrojejunostomy is the development of a gastrojejunal ulcer. The incidence of gastrojejunal ulcer in the series reported by Pollard *et al* [1] was 9.4 per cent. In the Druckerman *et al* series it was 4.8 per cent. The frequency of the other postgastrectomy complications is extremely difficult to estimate, but they are serious problems when they occur. Moore *et al* [1] in summarizing their experience with 155 subtotal gastrectomies reported unsatisfactory results in 23.9 per cent of patients. It has been these observations which have stimulated attempts to improve the postoperative surgical results for patients with peptic ulcer.

The operations of partial gastrectomy and vagotomy have been combined with encouraging initial results. Druckerman et al [3] have compared the results of treatment with subtotal gastric resection both with and without vagotomy. In the nonvagotomy group the incidence of gastrojejunal ulcer was 4.5 per cent, whereas the group having the combined operation did not develop any gastrojejunal ulcers in the series of 165 patients. The recurrence rate in the control series of 220 subtotal gastrectomies was 5.5 per cent. The mortality rate for the combined operation was 0.5 per cent and the only significant side effect was a moderate prolonged diarrhea in 7 per cent of the vagotomy–subtotal resection group.

no recurrences during the 5 year period were the same in both groups but that the recurrence rate and mortality rate were significantly less in the vagotomy with gastroenterostomy than in the resection group

Others who have used vagotomy extensively are also enthusiastic about it Crile ' [1] indicates that good or excellent results are achieved in 90 per cent of patients having vagotomy and gastroenterostomy He prefers this operation to gastric resection because of its lower mortality 0 5 per cent Crile believes that the postvagotomy complications can be minimized by proper placement of the stoma Diarrhea was the only significant complication in this series and it was rarely troublesome Dragstedt in summarizing the present status of vagotomy stated

> I advocate this operation because it is sound from the standpoint of abnormal physiology found in duodenal ulcer patients Many thousands of such patients are now living in comfort and free of ulcer disease as a result of vagotomy and gastroenterostomy Much of their comfort and ability to gain weight is due I believe to the fact that it has not been necessary to sacrifice the storage function of the stomach We are doing the operation with more enthusiasm and satisfaction than we did ten years ago Our experience has served to give us more confidence in the procedure If I had a duodenal ulcer myself that proved refractory to medical management I would not have three quarters or seven eighths gastric resection unless the more conservative operation had failed

Despite the apparent lower mortality of vagotomy and gastroenterostomy the majority of surgeons at the present time prefer a three quarters resection of the stomach completed by a short loop jejunostomy as treatment for duodenal ulcer The mortality rate of this operation varies consid

erably in the numerous reports in the literature Glenn and Harrison [3] report a mortality rate of 1 9 per cent with 87 per cent of their patients having satisfactory results following operation Eastman and Cole report a mortality rate of 5 8 per cent while others report rates of 2 86 per cent and 5 8 per cent [19]

The next most serious complication of gastrojejunostomy is the development of a gastrojejunal ulcer The incidence of gastrojejunal ulcer in the series reported by Pollard *et al* was 9 4 per cent In the Druckerman *et al* [5] series it was 4 8 per cent The frequency of the other postgastrectomy complications is extremely difficult to estimate but they are serious problems when they occur Moore *et al* [1] in summarizing their experience with 155 subtotal gastrectomies reported unsatisfactory results in 23 9 per cent of patients It has been these observations which have stimulated attempts to improve the postoperative surgical results for patients with peptic ulcer

The operations of partial gastrectomy and vagotomy have been combined [2] with encouraging initial results Druckerman *et al* have compared the results of treatment with subtotal gastric resection both with and without vagotomy In the nonvagotomy group the incidence of gastrojejunal ulcer was 4 5 per cent whereas the group having the combined operation did not develop any gastrojejunal ulcers in the series of 165 patients The recurrence rate in the control series of 220 subtotal gastrectomies was 5 5 per cent The mortality rate for the combined operation was 0 5 per cent and the only significant side effect was a moderate prolonged diarrhea in 7 per cent of the vagotomy-subtotal resection group

A similar approach to the problem is reported by Berne[9] who has suggested the combination of vagotomy pyloroplasty and large wedge resection of the body of the stomach The ulcer is left in place in this operation Long term results are not reported but the initial results seem favorable

Two other operations have been revived and modified in an attempt to eliminate the side effects of gastrojejunostomy in particular the dumping syndrome and nutritional deficiency Moore and Harkins[6,7] have reported on an extensive series of cases of duodenal ulcer treated by the Schoemaker modification of the Billroth I operation Their mortality rate for 127 patients was 2 4 per cent The incidence of presumed recurrent ulcer was 1 7 per cent Wangensteen[8] has proposed the use of segmental resection of the stomach preserving gastroduodenal continuity His initial results are reported as satisfactory although insufficient time has elapsed to form any definitive evaluation of this operation for gastroduodenal ulcer

From the summary of these conflicting opinions it seems apparent that there is no one best operation for gastroduodenal ulcer The type of surgery used must be individualized for the patient under consideration To a large extent the results reported appear to depend on the skill of the surgeon and the enthusiasm which he has for the particular operation Under these circumstances it is not possible to indicate the operation of choice but perhaps a combination of the several operations will ultimately offer the best long term results

Gastrojejunal Ulcer

Results of further surgical treatment for gastrojejunal ulcer are discussed in the section on postgastrectomy syndromes

POSTSURGICAL MANAGEMENT

An important aspect of the surgical treatment of peptic ulcer is the management of the immediate and late postoperative period Postsurgical management also includes the prevention and treatment of the postsurgical syndromes which may develop

It is frequently assumed by patients that if they undergo surgery no further medical treatment will be necessary It is true that medications can be discontinued after surgery but dietary restrictions should be continued for a variable period of time If the diet is liberalized too rapidly after operation symptoms may develop which are related to the altered size of the stomach and its lack of storage capacity Therefore the increments in the diet must be gradual rather than abrupt until the patient is able to eat three main meals a day with three intermediate feedings The patient should be followed carefully including x ray study for several years after surgery to make sure he does not develop recurrent ulceration of the stoma

POSTGASTRECTOMY SYNDROMES

The literature relating to postgastrectomy syndromes is both voluminous and confusing The confusion lies not so

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rapidly The normal stomach according to Machella [6] evacuates a mixed meal within a period of 3 or 4 hours at the rate of 10 to 15 cc per minute In patients with partial gastrectomy the gastric remnant is usually emptied within 10 to 30 minutes and it may empty within 5 minutes This has been employed as an argument for the wider adoption of the Billroth I resection wherein the gastric chyme leaves the stomach in a normal fashion

In their excellent discussion of the postgastrectomy syndromes Moore and Harkins [7] have classified the syndromes into six categories (1) recurrent or persistent ulceration including gastrojejunocolic fistula (2) the dumping syndrome (3) symptoms due to aberrations of carbohydrate absorption (4) postgastrectomy anemia (5) postoperative weight change and (6) miscellaneous syndromes

Recurrent or Persistent Ulceration

The incidence of recurrent ulceration after an adequate gastrectomy is difficult to estimate It is thought that 5 to 10 per cent of patients develop marginal ulcers after adequate gastrectomy It is more common after gastroenterostomy or inadequate gastric resection The time of development of a marginal ulcer after surgery is variable and may range from a few days after operation to 20 or more years Marginal ulcers usually develop within 3 to 5 years after operation They are commoner in men than in women

Marginal ulcer is thought to be related to the excessive hydrochloric acid in duodenal ulcer patients It almost never follows surgery for gastric ulcer where hypersecretion is not a problem Marginal ulcer is more prone to occur when the stomach is anastomosed to the jejunum than to the duo

much in the description of the syndromes as in the explanations regarding the mechanism of production of the patterns In addition to recurrent ulceration with development of a gastrojejunal ulcer and in rare instances a gastrojejunal colic fistula a considerable percentage of patients develop symptoms which are related to the ingestion of food Zollinger and Hoerr indicate that such symptoms may occur in as many as 25 per cent of postresection patients

A better understanding of the postgastrectomy syndromes may be secured by a brief review of the physiology of the normal and the subtotally resected stomach Moore and Harkins have discussed this problem under six headings (1) reservoir function (2) influence of bacterial flora (3) mixing and morcellation of food and protein digestion (4) controlled release of gastric chyme into the intestine (5) iron absorption (6) intrinsic antianemic factor

Modifications of function take place in the resected stomach as compared with the normal stomach The reservoir capacity of the stomach is decreased to about 25 per cent of normal This is accompanied by more rapid evacuation of the food from the stomach Many patients who have had a subtotal gastrectomy learn to avoid the ingestion of large meals because of the resultant feeling of fullness nausea and even vomiting

Subtotal resection also influences the bacterial flora of the intestinal tract as a result of the production of hypochlorhydria or achlorhydria This change in the bacterial flora may have a relation to the development of diarrhea and steatorrhea after gastrectomy

The mixing and morcellation functions are lost after subtotal gastrectomy and the food leaves the stomach more

Treatment should be initiated as soon as the diagnosis of gastrojejunal ulcer is suspected Medical treatment is worthy of a thorough trial but is frequently not effective and surgery must be considered An example of a marginal ulcer following gastroenterostomy and vagotomy is given in the following case

> J K a 49 year old man had duodenal ulcer for 4 years Despite adequate management he was never symptom free and had severe semiannual recurrences Vagotomy and gastroenterostomy were performed in 1953 He developed recurrent low epigastric pain after meals X ray showed a large stomal ulcer (Fig 29) Gastric resection was required

The type of surgical treatment to be performed depends upon what type of surgery was performed in the past In the presence of a previous gastroenterostomy most surgeons recommend that the gastroenterostomy be taken down and an adequate gastric resection of either the Billroth I or II type be performed Vagotomy may be performed at this time in addition to gastric resection If a marginal ulcer followed an adequate gastric resection it is recommended that the ulcerated area be resected and that a vagotomy be performed

Gastrojejunocolic fistula is a rare complication which occurs in approximately 5 per cent of patients who develop a marginal ulcer The symptoms and signs are characteristic — a sudden onset of diarrhea with the passage of undigested food particles rapid loss of weight and the development of edema Symptoms of gastroenteritis may result from leakage of fecal matter into the stomach and jejunum The diagnosis can usually be confirmed by x ray The barium enema will demonstrate the connection between the colon small

denum the mucosa of the jejunum being less resistant to acid digestion The anastomosis of the stomach to the jejunum stimulates acid secretion more than the performance of a gastroduodenostomy

Marginal ulcers are usually located on the small bowel side of the anastomosis in the direction of the efferent loop The crater is small and frequently surrounded by edema inflammation and adhesions Edema may reduce the size of the stoma so that obstruction occurs Penetration of adjacent tissue is common and if this involves the layers of the transverse mesocolon a gastrojejunocolic fistula may result

The most important symptom of marginal ulcer is pain which differs from the previous ulcer pain It is more severe and is located to the left and downward from the site of the original pain The pain may have a relationship to meals but if the ulcer penetrates or perforates the relationship to meals may be lost Bleeding obstruction perforation and fistula formation may all occur

X ray studies are of some help in the diagnosis It may be possible to outline the niche of a stomal ulcer or to elicit tenderness by palpation over the stoma The demonstration of a stomal ulcer is difficult and it is probable that not more than a third of patients having the clinical features of a stomal ulcer show x ray evidence of such an ulcer Many ulcers are seen at side view presenting a slitlike appearance or they may be entirely hidden from view by barium in the normal mucosal folds or in the suture lines

Gastroscopy is of little help in the diagnosis The stoma may be visualized but the ulcer can rarely be seen as it is on the distal side of the anastomosis Edema of the stoma or bleeding may be observed

bowel and stomach more readily than an upper gastrointestinal series Gastrojejunocolic fistula must be differentiated from the similar symptoms which accompany the inadvertent performance of a gastroileostomy

After correction of dehydration and malnutrition surgical treatment of the fistula can be initiated The most satisfactory operative procedure divides the fistula closing the opening into the colon This is followed by resection of the stomal ulcer in a manner similar to that employed with patients with marginal ulcer

The Dumping Syndrome

The dumping syndrome may be defined as the occurrence of sweating unpleasant warmth flushing nausea palpitation diarrhea and faintness which has its onset shortly after ingesting a meal It may last up to 45 minutes after a meal and is relieved by lying down Custer *et al* [8] reviewed 500 routine consecutive cases of subtotal gastric resection performed at the Mayo Clinic between 1935 and 1938 They found an incidence of 5 6 per cent of the dumping syndrome in this series In reviewing another series in which the dumping syndrome was looked for the incidence was found to be 12 5 per cent

The mechanism of the development of the dumping syndrome is not clear Perman has pointed out that the incidence of the dumping syndrome increases with the extent of the resection It is thought therefore that the syndrome is due to a rapid uncontrolled emptying of large amounts of unprepared food into the small intestine Meals with large carbohydrate content especially concentrated carbohydrate are most likely to provoke an attack Machella has simu



FIGURE 29

Billroth I procedure [7] The Billroth II type of anastomosis is sometimes converted into the Billroth I in an attempt to relieve a severe dumping syndrome In order to achieve adequate restoration of gastroduodenal continuity interposition of a small jejunal loop after the method of Henley has proved to be helpful [1]

Symptoms Due to Alterations of Carbohydrate Absorption

Alterations in carbohydrate metabolism may occur after gastrectomy These appear to be the result of the early evacuation of the stomach which leads to rapid absorption of glucose from the small bowel This may be followed by hypoglycemia in a period of 2 to 3 hours The manifestations of the hypoglycemic attack are hunger weakness sweating tremors blurred vision palpitations paresthesias and psychic disturbances [3] Hard physical exercise is usually the precipitating factor and in each instance a small carbohydrate meal will abolish the symptoms completely

Symptoms due to alterations of carbohydrate absorption are infrequently seen and seldom lead to significant disability When they do occur the treatment consists of a high protein diet, which minimizes the fluctuations of the blood sugar concentration

Postgastrectomy Anemia

Iron absorption is decreased following the performance of gastric resection The poor absorption is caused by the rapid emptying of the gastric segment The presence of achlorhydria may be a contributing factor but it does not appear to be the most important one as iron absorption is satisfac

lated this syndrome by instilling protein hydrolysate or magnesium sulfate into the jejunum He proposed that the symptoms were produced by distention of the jejunum and that the distention was ordinarily produced by the outpouring of fluid from the jejunum in an attempt to make the hypertonic contents isotonic

Recommendations have been made in regard to the treatment *of the dumping syndrome Perman* [9] *suggested that* the patient be encouraged to chew food well to avoid drinking fluids during the meals and to eat while lying on the left side in order to control the tendency towards rapid emptying of the stomach

Other factors may influence the development of the *dumping syndrome It has been reported that the symptoms* can be relieved by thoracolumbar sympathectomy [1] and by *ganglionic blocking agents* [31] *The ganglionic blocking agents* act to slow down the increased motor activity of the intestine resulting from the passage of unprepared food to the jejunum [31] The selection of patients for surgery appears to influence the incidence of postgastrectomy symptoms especially the dumping syndrome The symptoms of the dumping syndrome are almost identical to those produced by anxiety and the syndrome appears to be more frequent in obviously neurotic individuals

The dumping syndrome is influenced by the size and type of the gastroenteric anastomosis The incidence of the syndrome is less when the Hofmeister modification of the Polya operation is used or when the Schoemaker modification of the Billroth I is used The incidence of the dumping syndrome in the Billroth I and Billroth II procedures was the same but the severity of the symptoms was less with the

been performed the reflux of alkaline juices into the gastric pouch producing a chronic alkaline gastritis Nausea is a bothersome symptom and this may be combined with difficulties in emptying Diversion of the alkaline juices away from the stomach may have to be performed

POSTVAGOTOMY SYNDROMES

Symptoms may follow the performance of a vagotomy although they are usually not as serious a problem as the postgastrectomy syndromes Recurrent or persistent ulceration has been noted in patients who were treated with vagotomy and gastroenterostomy Some of these patients have had to be reoperated upon having a gastric resection in addition to their vagotomy It is thought that the poorer results with the development of recurrent ulceration may be indicative of an incomplete vagotomy The Hollander test which measures the effect of hypoglycemia on gastric acidity can be used to determine the completeness of vagotomy If the operation is complete the administration of insulin usually 15 units with the resultant fall in blood sugar to 50 mg per cent or below does not stimulate the production of free hydrochloric acid If the vagotomy is incomplete the hypoglycemia produced by the injection of insulin will stimulate the production of free hydrochloric acid indicating that the cephalic phase of secretion has not been abolished

Other symptoms have been reported by patients following vagotomy These consist of heartburn fullness after meals abdominal pain and intractable diarrhea Most of these symptoms are related to the disturbances in motility and gastric evacuation following performance of vagotomy

tory even in the presence of achlorhydria The condition is rare in men occurring most frequently in menstruating women It is less common with the Billroth I procedure than with the Billroth II

Postoperative Weight Change

One of the problems that resected patients frequently have is difficulty in gaining weight in the postoperative period Increased fat is lost in the stool after resection This fat loss is higher with the Billroth II operation than with the Billroth I

Zollinger and Ellison[33] *studied postoperative weight* change in 203 ulcer patients subjected to a variety of standard surgical procedures Patients who were underweight prior to the development of their ulcer tended to have weight problems after resection Satisfactory nutrition could be anticipated in two thirds of patients who were of normal weight or overweight regardless of the procedure used Zollinger and Ellison suggested that more conservative procedures be employed in patients who were underweight prior to their illness either 60 per cent Billroth I resection with vagotomy or vagotomy and posterior gastroenterostomy

Miscellaneous Syndromes

*Vitamin deficiencies have been reported after gastric re*section Patients should have vitamin supplements because of faulty absorption particularly of the fat soluble vitamins after gastrectomy

Another problem which occurs after gastrectomy is gastritis This is likely to occur when a very high resection has

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alone The use of gastric suction in the immediate postop erative period and the concurrent performance of gastro enterostomy pyloroplasty or partial gastric resection has largely eliminated these symptoms

Even with the performance of a secondary drainage op eration and with the proper development of a stoma a cer tain percentage of patients develop diarrhea following va gotomy The cause of the diarrhea is not known but it is thought that possibly it is due to the altered motor function of the stomach and upper small bowel It occurs in about 7 per cent of patients It can be treated with the general measures which are used for treatment of nonspecific diar rhea

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tistics from 1 per cent to more than 20 per cent If patients with ulcerating carcinoma can be differentiated from patients with benign ulceration surgery will not have to be performed on patients with benign gastric ulcers solely because of fear of carcinoma

DIFFERENCES BETWEEN GASTRIC AND DUODENAL ULCERS

Although gastric and duodenal ulcers are similar in many ways there are important differences Gastric ulcer appears to be less common than duodenal ulcer when the estimates of frequency are based upon radiologic statistics At autopsy the incidence of the two diseases is identical[2] The difference in incidence may be explained by the fact that many gastric ulcers present bizarre symptoms and are not recognized clinically The actual incidence of gastric ulcer would appear to be greater than the clinical data now indicate Gastric ulcers also differ from duodenal ulcers in that they tend to appear at a somewhat later age than duodenal ulcers

The etiologic factors underlying gastric and duodenal ulcer also differ The mean gastric acid response in gastric ulcer patients is lower than in normal individuals and considerably lower than the elevated values seen in duodenal ulcer patients The development of a gastric ulcer in a patient who previously had a duodenal ulcer may be accompanied by a fall in gastric acidity The pathogenesis of gastric ulcer seems to be related more to a decreased mucosal resistance of the stomach than to overactivity of the aggressive acid pepsin interaction

14

GASTRIC ULCER AND THE ULCER-CANCER PROBLEM

The management of the patient with a gastric ulcer is an extremely controversial subject with wide differences of opinion being voiced by the surgeons and the internists Some surgeons recommend that all gastric ulcers regardless of their location or clinical features be removed Most gastroenterologists on the other hand feel that gastric ulcer is primarily a medical problem and that the results of medical treatment are good If the ulcer does not heal or if there is a suspicion of malignancy most gastroenterologists would recommend that the patient be referred to the surgeon for treatment [1] All gradations of opinion can be found between these two extremes

Why does gastric ulcer present so many difficulties to the clinician and why is it such a controversial subject? The major problem is the differential diagnosis between benign gastric ulcers and ulcerating carcinomas which simulate benign ulcers The incidence of gastric carcinoma presenting as an apparently benign ulcer ranges in the reported sta

16 per cent Marshall and Welch reported 19 8 per cent of *apparently benign gastric ulcers to be malignant*[4] while others have reported figures ranging from 10 to 16 per cent[5 6 7]

Browne *et al* indicate that if gastric ulcer patients are studied carefully with the specific aim of excluding patients *who have malignant ulceration the error in diagnosis* should be very small A series of 200 patients were followed utilizing a definite program for the specific purpose of care fully differentiating those patients who required surgical in tervention from those with a benign uncomplicated ulcer It *was found that the error of misdiagnosing malignant lesions* was low being only 1 per cent Browne *et al* emphasized the value of exfoliative cytology in diagnosis of the ulcerat ing lesion of the stomach in addition to the usual diagnostic studies

DIAGNOSIS OF GASTRIC ULCER

The diagnosis of gastric ulcer is based upon the clinical features presented by the patient careful x ray study of the lesion the gastroscopic findings and the study of exfoliated cells from the stomach

Clinical Features

The clinical features of gastric ulcer although similar to those of *duodenal ulcer are less characteristic The gnaw* ing distress has a less definite relation to meals Moynihan attempted to utilize the relationship of distress to meals in an effort to differentiate clinically between gastric and duodenal ulcer (See Chapter 5)

Alterations in the motor function of the stomach are common in patients with gastric ulcer particularly if the ulcers are located in the distal half of the stomach Delay in gastric emptying with resultant gastric retention is a common occurrence The opposite change is also seen that is increased gastric peristalsis and evacuation

RELATION TO GASTRIC CANCER

It was formerly believed that gastric ulcers might develop malignant degeneration This was based primarily on the finding of malignant changes on one side of an otherwise benign ulcer There is no proof that malignant change takes place and most observers now believe that malignant ulcers were malignant from the beginning and not the result of a malignant degeneration of a previously benign lesion One of the difficulties in this problem is that we know so little about the natural history of malignancy There are well documented cases wherein tumors were present for many years without causing metastatic change This may be related to the problem of carcinoma *in situ* where one has evidence of cytologic alterations without the presence of metastases which are the usual accompaniment of a malignant tumor

The reported incidence of malignant ulcer in patients having an apparently benign gastric lesion varies considerably Smith *et al* [3] reporting on 1000 patients with the clinical diagnosis of benign gastric ulcer after excluding obvious malignancies observed that 8 8 per cent of these patients ultimately were found to have malignant ulceration The incidence of malignancy in patients with recurrent ulcer was

FIGURE 30

X rays of a channel ulcer (From Texter *et al* Reproduced with kind permission of the editor of *Gastroenterology*)



FIGURE 31

X rays of a channel ulcer (From Texter *et al* Reproduced with kind permission of the editor of *Gastroenterology*)

The degree of distress presented by the gastric ulcer patient depends upon the size and location of the ulcer If the gastric ulcer is superficial in location pain may not be present and many gastric ulcers are not recognized clinically If the ulcer becomes deeper poorly localized pain may be reported

Ulcers located high in the stomach may be entirely asymptomatic Ulcers located below the incisura angularis are more likely to present symptoms If the ulcer is located in the pyloric channel area bizarre symptoms are frequently present The most common complaints of patients with channel ulcer are nausea and vomiting which occur in 80 per cent of these patients [10] Eusterman has termed this the *syndrome pylorique* [11] Atypical pain is also common in patients with pyloric channel ulcer It may be so severe as to require narcotics for relief The pain along with the weight loss which is frequently present may suggest that the patient has carcinoma This problem is illustrated by the following case

J T a 50 year old woman was hospitalized five times within 10 months because of abdominal pain nausea and vomiting along with weight loss Admission diagnosis was carcinoma of the stomach X ray (9/19 52) showed persistent narrowing of the antrum and gastroscopy revealed evidence of recent bleeding Repeat x rays (10 9/52) showed scarring of the antrum (Fig 30) Re examination (11/18/52) showed a small crater projecting from the lesser curvature of the pyloric channel which later increased in size (12 17 52) (Fig 31) She made an uneventful recovery following gastric resection The ulcer was benign

The clinical features of the patient with a gastric ulcer may be altered if complications are present Gross bleeding

FIGURE 30

X rays of a channel ulcer (From Texter *et al* Reproduced w th kind permission of the editor of *Gastroentero o y*)



FIGURE 31

X rays of a channel ulcer (From Te ter *et al* ° Reproduc d with kind permission of the ed tor of *Gast ocnterolog*)

is common in patients with gastric ulcer Hematemesis is a more frequent occurrence in the gastric ulcer patient than in patients with duodenal ulcer The hematemesis is usually of large quantity which is of value in differentiating bleeding from a benign source from bleeding from malignancy as the latter is usually of small amount

Perforation both free and walled off may occur Free perforation is accompanied by sudden severe abdominal pain with boardlike rigidity of the abdomen If the perforation becomes walled off to the pancreas or other adjacent structures the pain pattern is altered The pain usually becomes more severe and radiates directly through to the back Occasionally walled off perforations become adherent to the liver and the patient may notice that the pain is affected by respiration

Physical examination is of less value than the history in establishing the diagnosis One may elicit areas of localized tenderness if the ulcer is located anteriorly in an area which is accessible to palpation Many ulcers are inaccessible to palpation particularly those located in the upper portion of the stomach

Laboratory Examination

Laboratory studies including gastric analysis stool examination for occult blood and the study of exfoliated cells from the stomach are extremely helpful in differentiating patients with benign gastric ulcer from those with ulcerating malignancy The gastric analysis per se is of little value in differentiating ulcerating malignancy from benign ulcer as the majority of patients with carcinoma have no free acid However the persistent failure to demonstrate acid

after histamine stimulation in the presence of a gastric crater strongly suggests that the lesion is malignant[1]

Examination of the stool for occult blood is an aid in distinguishing between patients with benign and malignant lesions The persistence of occult blood in the stool is unusual in patients with benign gastric ulcer If occult blood is persistently present even after the patient is placed on a meat free diet it is highly suggestive that the patient has a malignant process

The application of the Papanicolaou technique of study of exfoliative cells from the gastric mucosa has been a distinct advance in our efforts to distinguish benign ulcer from malignancy Malignancy can frequently be recognized from changes in the cells themselves even though the usual additional characteristics of invasiveness and metastasis are absent Cells can be obtained by lavage with Ringer s solution the collected material being centrifuged and smeared on slides coated with serum for subsequent staining and study The exfoliated cells can be embedded in paraffin and sectioned in a manner similar to the usual microscopic sections This technique has limited diagnostic accuracy being positive in only 20 per cent of patients having known gastric carcinoma [3]

Abrasion of the anterior of the stomach can be used to increase the amount of cytologic material available for study Abrasive balloons have been used by Panico *et al* [3] Rubin *et al* and others while Ayre and Oren employ a rotating brush The frequency of positive cytologic identification of carcinoma has been increased to about 85 per cent with this approach

Mucolytic agents including papain and chymotrypsin

can be employed to extend the usefulness of exfoliative cytology. The results following the instillation of mucolytic agents without the use of the abrasive balloon appeared to be about as accurate as the balloon method and considerably simpler to carry out.[19]

The basic procedure is similar for the several variations in technique. The patient should be fasting for 12 hours before the study. If any obstruction is present, preliminary lavage or the use of a liquid diet for several days prior to study is necessary to eliminate food particles which render the interpretation of the slides difficult. The stomach is lavaged with Ringer's solution and the collected material aspirated and centrifuged. The material must be collected rapidly on ice so that acid autolysis does not occur. After this either an abrasive balloon is inserted or one of the mucolytic agents is instilled and material is obtained after completion of these procedures.

The value of exfoliative cytology in the differential diagnosis of lesions of the stomach has been amply demonstrated, particularly in the series of cases reported by Browne *et al.* The technique does have limitations. It is time consuming both to obtain the material and to scan the slide adequately. There is also a shortage of personnel trained in the study of exfoliated cytologic material. A partial solution to this problem may be the development of semiautomatic scanning techniques. Such a technique as developed by Mellors *et al.* and Trolles[1] makes use of the fact that cancer cells contain larger nuclei than do normal cells. If exfoliated cytologic material is stained with a fluorescent type of dye, an automatic scanning device can be used to screen out negative slides. Suspicious or positive

slides having increased fluorescence are reserved for special individual study

Gastroscopy

Gastroscopy is of help in distinguishing benign from malignant gastric lesions The gross characteristics of the two lesions usually differ markedly In benign gastric ulcer the gastroscopist observes a punched-out ulcer with smooth edges and a clean looking base Gastroscopically visible bleeding is infrequent This is in contrast to the irregularities which are seen when the malignant ulcers are studied gastroscopically The edges are usually nodular and the base is shaggy and has less of the punched out appearance of benign ulcer Bleeding from the lesion is more likely to be seen with malignant lesions than with a benign ulcer The accuracy of gastroscopy particularly when used in conjunction with x ray is high Baker *et al* found that 91 5 per cent of gastric neoplasms were diagnosed correctly preoperatively when gastroscopy was combined with x ray

Biopsy of intragastric lesions is also possible Operating gastroscopes devised by Benedict and Tomenius are available in addition to the biopsy techniques utilized by Wood Sizable areas of the stomach are in gastroscopically blind areas and are not accessible to biopsy The gastroscopist may not be able to obtain an adequate view of the lesion and cannot biopsy it very satisfactorily Gastroscopy including biopsy is of most value when used as an adjunct to consideration of the clinical features and x ray appearance

X Ray Diagnosis

X ray study is the most valuable single diagnostic technique for the diagnosis of gastric ulcer even though it has limitations A gastric ulcer may escape observation by the roentgenologist This may occur if the crater is filled with mucus or blood clot or if the crater is located in an area inaccessible to palpation and is therefore difficult to demonstrate Gastric ulcers also may be missed because of misinterpretation of the films Both these errors should be small when the study is being performed by a skilled radiologist The most serious error is misdiagnosing gastric cancer as a benign gastric ulcer Ten to 15 per cent of gastric ulcers have gross x ray characteristics of benign ulcer and yet are found to be malignant on microscopic study

The principal roentgenologic sign of benign gastric ulcer is the barium filled excavation produced by the ulcer which is recognized as a crater This may be accompanied by secondary x ray findings such as localized spasm change in the mucosal relief pattern tenderness on palpation and evidence of gastric retention

Three quarters of all gastric ulcers occur in the region of the lesser curvature They may be located on either the adjacent anterior or posterior wall Most lesser curvature ulcers are close to the incisura angularis

The prepyloric area is a common site for benign ulcers with 20 per cent of gastric ulcers being located in this area Ulcers below the incisura angularis are more difficult to demonstrate than those above Spasm of the antrum and roentgenologic evidence of gastritis are frequent with prepyloric ulcers Prepyloric ulcers may be confused

with duodenal ulcer and also with carcinoma involving this area Prepyloric ulcers must be differentiated from hypertrophy of the pyloric muscle and from pyloric channel ulcers

Between 5 and 10 per cent of gastric ulcers occur in the cardiac portion of the stomach Ulcers in this area are difficult to diagnose because they are inaccessible to palpation The first suspicion of an ulcer may be the recognition of secondary signs of ulceration elsewhere in the stomach Careful demonstration of the cardia including the use of a carbonated barium mixture may be necessary Ulcers in the cardia must be differentiated from carcinoma diverticula and rarely from benign neoplasms

Benign ulcers are seldom located on the body or greater curvature of the stomach only 3 per cent of all gastric ulcers being found there [6] The majority of ulcerating lesions of the greater curvature and body of the stomach are malignant Benign ulcers can occur in this area and present many difficulties in differential diagnosis This is illustrated by the following case

O G a 65 year old white male had a gastric ulcer in 1950 which responded well to medical management Routine follow up in 1951 (when the patient was asymptomatic) revealed recurrent greater curvature ulcer loss of pliability and gastric residual Gastroscopy showed antral gastritis There was no occult blood Laparotomy revealed a chronic benign ulcer which was resected (Fig 32)

Approximately 12 per cent of benign ulcers originate in the pylorus The x ray signs of pyloric channel ulcer are demonstration of a crater projecting from the pyloric channel and distortion shortening or lengthening of the pyloric



FIGURE 32

channel area Gastric retention is frequently present Pyloric channel ulcers must be differentiated from duodenal ulcer located in the juxtapyloric area hypertrophy of the pyloric muscle and carcinoma of the prepyloric segment of the stomach Carcinoma originating in the pylorus is extremely rare

The major problem confronting the roentgenologist is differentiating the 15 per cent of ulcerating malignancies that resemble benign gastric ulcer Formerly it was thought that size was valuable in differentiating benign from malignant lesions It has been shown that this is not a very useful criterion

There are roentgenologic criteria suggestive of malignancy The previously described meniscus effect of the "crater on top of the hill" may be observed Alterations in the pliability and flexibility of the stomach in the presence of malignancy are common The response to therapy is useful to the roentgenologist Even though malignant ulcers may show some improvement and decrease in size they do not go on to complete healing such as occurs with benign ulcer However if the benign ulcer is walled off and perforated it may not heal despite the best medical management as illustrated by the following case

J B a 69 year old white male had massive hematemesis from gastric ulcer in 1948 He had persistent pain with recurrent melena and a second massive hemorrhage in 1954 there was also weight loss Free hydrochloric acid was present X rays showed a large lesser curvature ulcer with 50 per cent gastric retention in 4 hours (Fig 33) There was minimal change in 2 weeks of management Laparotomy revealed a benign chronic peptic ulcer which was adherent to adjacent structures



Figure 33
X ray of a large benign gastric ulcer on the lesser curvature

Gastric ulcers heal rapidly, although the rate of healing depends on their location and their size and depth. The average healing time is 40 days, and x-ray studies should be carried out at weekly to biweekly intervals to evaluate the results of treatment. Apparent healing is not an infallible indication of a benign lesion, and certain malignant ulcers show x-ray evidence of healing only to recur at a later date.

The x-ray signs of gastritis may resemble those of ulcer except that a crater cannot be demonstrated. This is particularly true if the gastritis is located in the prepyloric segment. Gastroscopic examination can be a definite aid in this situation.

TREATMENT OF GASTRIC ULCER

Both medical and surgical treatment are used to treat gastric ulcers. The practical problem in the type of treatment to be employed concerns the ability of the clinicians to distinguish between benign and malignant ulcers of the stomach, utilizing all aids short of a histologic examination of the resected specimen. Zetzel has summarized the arguments in favor of immediate operation for all gastric ulcers as follows: (1) There has been little improvement in the survival rate of patients with carcinoma of the stomach, due primarily to failure to make a diagnosis and obtain surgical care before metastases have occurred. (2) Radical resection in all cases with gastric ulcer before the diagnosis of cancer becomes obvious may salvage an appreciable number of cases early, even though many patients thus treated cannot be proved to have a malignant ulcer. (3) One cannot make a distinction between benign and malignant ulcer

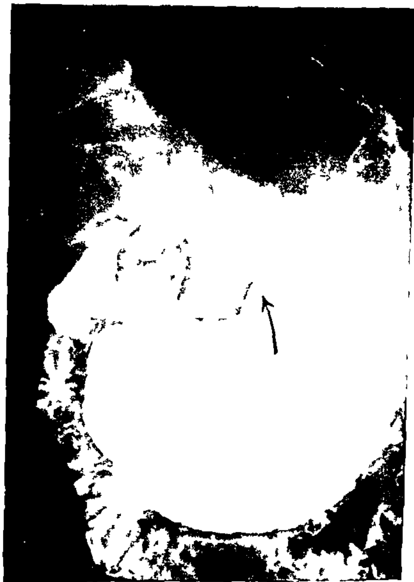


FIGURE 33
X ray of a large benign gastric ulcer on the lesser curvature

Medical Treatment

Patients with gastric lesions should be hospitalized and maintained in the hospital until complete healing takes place or until the decision can be made whether they are to be treated surgically The general principles of treatment of gastric ulcer are similar to those of duodenal ulcer (See Chapter 7) Additional responsibility is placed on the physician however to be quite certain that the lesion under treatment is actually a benign ulcer rather than an ulcerating malignancy

There is some difference of opinion between physicians and surgeons as to the length of time that should be allotted to a trial of medical management Smith *et al* feel that a month or less of intensive management is justified in many cases of gastric ulcer No hard and fast rules can be set up and the length of time should be individualized in each patient

Surgical Treatment

If healing of the gastric ulcer does not take place promptly on intensive medical management surgical intervention is indicated The operation of choice is a gastric resection including the resection of the ulcer

RESULTS OF TREATMENT

There are marked differences in the reported end results of treatment for the gastric ulcer patient Smith *et al* have reviewed their experience with 1000 cases of apparently benign gastric ulcer A total of 912 of these patients had be

with sufficient accuracy to permit conservative treatment and continued observation (4) The results of gastric resection for gastric ulcer are uniformly good the mortality rate and incidence of recurrences low and lastly to delay surgery until the results of medical treatment which are equivocal to begin with can be evaluated is hazardous as far as the optimum time for resection is concerned

There are also arguments against immediate surgical intervention [9] The patient with a gastric ulcer if he is to be treated properly must be educated to the necessity for continuing treatment with participation by both the physician and the patient Although there are no diagnostic criteria which are 100 per cent indicative of a benign lesion the complete remission of all ulcer signs and symptoms the disappearance of roentgenologic evidence of ulceration and rigidity of the wall as demonstrated by x ray and gastroscopy the presence of free acid and the disappearance of occult blood from the stool all suggest that the patient has a benign lesion Inasmuch as incidence of success in the 5 year cure for carcinoma is so low anyway a delay of 4 to 6 weeks would not appreciably alter the ultimate results if healing did not take place on a conservative program If however the patient has persistent achlorhydria to histamine a positive Papanicolaou test on gastric washings a meniscus sign on x ray or an ulcer on the greater curvature or in the prepyloric region immediate operation should be advised It appears that the diagnostic error of mistaking an ulcerating malignancy for a benign lesion would be at least as low as the usual surgical mortality namely 3 to 5 per cent and in the experience of some the error in diagnosis has been as low as 1 per cent

pital in London followed 387 men and 111 women with *chronic gastric ulcer during the period 1940–1946* Roughly one half of the patients 262 were treated medically while the remainder had gastric surgery performed The criterion for inclusion of patients in the study was presence of an active chronic gastric ulcer which in the medical series was seen gastroscopically The indications for surgery were primarily pyloric obstruction or failure of medical management The minimum follow up period was 5 years the maximum 12 Surgical mortality for partial gastrectomy was 6 3 per cent Cancer developed in 15 medically and 11 surgically treated patients In 10 of these 26 patients the primary growth was probably in the stomach Symptoms of gastric ulcer recurred in three quarters of the medically treated patients It was concluded that medical treatment might heal *the ulcer but would keep it healed in less than one quarter* of the earlier or milder cases Patients with a short history prior to diagnosis responded slightly better to treatment but their chances of remaining symptom free were still less than 50 per cent Satisfactory results were obtained in 80 per cent of the surgically treated patients moderately successful results in 10 per cent and poor results in the remaining 10 per cent There were no instances of marginal ulcer following gastrectomy In comparing the two series they noted that one fourth of the patients in the medical series as compared to over three fourths in the surgical series had no further trouble

It is difficult to reconcile the conclusions of these several reports Ingelfinger[a] commenting on this has pointed out that *the medical treatment of gastric ulcer is justified in* many cases that the results of surgery are satisfactory in 80

nign ulcers and 88 patients had malignant gastric ulcers Slightly over half the patients were operated upon — 497 with benign ulcer and 81 with malignant ulcer Suspicion of cancer was a major indication for surgery Follow up studies on 380 patients with benign lesions treated by resection showed that 78 7 per cent had good results 14 2 per cent fair results and 7 1 per cent poor results Of the 397 patients with benign lesions treated medically 75 1 per cent had good results 13 8 per cent fair results and 11 1 per cent poor results The follow up periods varied from 2 months to 29 years There was little difference in mortality or morbidity between the medically and surgically treated groups The over all incidence of malignancy in this group of patients with apparently benign ulcer was 8 8 per cent but among those patients who had recurrent ulcer 16 per cent of cases were malignant

A less optimistic report was presented by Banks and Zetzel who studied the clinical course and late results of medical management of gastric ulcer in 48 patients These patients were followed for periods ranging up to 15 years Of the 38 patients available for follow up only 11 were symptom free during the follow up period Seven patients had one or more recurrences and 20 patients continued to have periodic exacerbations Eight of this group died of carcinoma of the stomach The report concluded that recurrences may be expected to occur in 50 to 90 per cent of patients with gastric ulcer during a 5 year follow up and therefore it was felt logical to recommend gastric resection promptly to protect the patient both from recurrences and from the jeopardy of cancer

Swynnerton and Tanner reporting from St James s Hos

indicate that neoplastic transformation takes place so that a benign lesion becomes a malignant ulceration The problem then is one of differentiating an ulcerating malignancy from benign gastric ulcer Our position on this problem is essentially the same as Palmer s He stated

> The practical diagnostic and therapeutic difficulty may be resolved by the immediate removal of all gastric ulcers — the procedure favored by most surgeons and many internists Those of us who essay to treat gastric ulcers medically as benign lesions must accept a certain risk just as a surgeon does in operation The amount of this risk is a matter of opinion rather than a fact Medical treatment is permissible only if exhaustive study fails to disclose evidence of neoplasm it may be continued only if the objective methods of x ray and gastroscopy show healing of the ulcer with no infiltration The treatment of gastric neoplasm is entirely surgical

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per cent of cases but that the mortality rate of the operation is still far from negligible that the recurrent ulcer is considered a strong indication for operation because of fear of malignancy and also because recurrence indicates that the ulcer is intractable to medical management and lastly that the most serious mistake is to discharge the patient with a gastric ulcer from the hospital without radiologic evidence that the ulcer has disappeared The physician has a great obligation to follow the subsequent course of a medically treated gastric ulcer patient to be certain that recurrences do not develop and that the ulcer is actually healed

The location of the ulcer may also influence the results of treatment Ulcers located below the incisura and particularly the pyloric channel area appear to do less well on medical management Repeated hospitalizations are necessary for patients with channel ulcers and despite intensive medical treatment satisfactory recovery is not the rule being observed in only 16 per cent of a series of 55 patients followed [1] Forty seven per cent of these patients had gastric surgery performed primarily because of pyloric obstruction or the failure of medical management The remaining 37 per cent of this group continued to have symptoms and periodic recurrences Surgery was advised for the majority in this group None had carcinoma which supports the observation that while carcinoma is frequent in the prepyloric area it does not involve the pyloric area except by extension

The management of the patient with gastric ulcer is difficult because peptic ulceration may develop either in normal mucosa or in neoplasm The pathology of the ulcerating carcinoma may be determined more by the peptic ulceration than by the actual neoplasm There is no evidence to

APPENDIX

Recipes for Foods Commonly Used in Peptic Ulcer Management

SCRAMBLED EGGS

Heat on low heat 1 teaspoonful of butter for each egg in a frying pan. Beat the eggs until the whites and yolks are well mixed. Season with salt and add 1 to 3 tablespoonfuls of milk or cream for each egg. Pour into hot butter and cook slowly, stirring constantly until eggs are done as desired. Serve at once.

PLAIN OMELET
(Yield 2 servings)

[illegible] eggs	1 tsp. butter
[illegible] Tbsp. milk	[illegible] taste

Beat eggs well [illegible] add milk and salt. Melt butter [illegible] on low heat in a frying pan. Add eggs [illegible] and cook [illegible] [illegible] [illegible] the eggs [illegible] Cook in a slow oven [illegible] F. for 10 [illegible] minutes. [illegible] grated [illegible] cheese [illegible] [illegible] [illegible] [illegible] Remove [illegible] Serve at once on a warm plate.

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PLAIN OMELET

(Yield 2 servings)

3 eggs	1 tsp butter
3 Tbsp milk	Salt to taste

Beat eggs well. Blend with milk and salt. Melt butter on slow heat in a frying pan. Add egg mixture and cook slowly on top of the stove until the eggs in the bottom are set. Cook in a slow oven (325 F) for 10 minutes. If desired, grated mild cheese, asparagus, mushrooms, peas and so forth may be placed in the middle before it is folded over. Remove, fold carefully in half. Serve at once on a warm plate.

EGGNOG

(Yield 1 large glass)

1 egg	1½ tsp sugar
¾ cup milk	¼ tsp vanilla

Pinch of salt

Scald milk in double boiler Pour slowly over well beaten egg stirring constantly Add sugar salt and vanilla Chill thoroughly

SOUPS

Cream soups are desirable for the peptic ulcer patient Soups should not be made with meat stock

(Yield 1 cup)

Add ½ cup of vegetable puree to the thin white sauce recipe (see White Sauce table page 271) Cook for 20 minutes in a double boiler Stir occasionally If the soup is thicker than desired it may be thinned by adding milk or vegetable water

Puree may be made by cooking fresh frozen or canned vegetables in a small amount of boiling water or in a pressure cooker until tender When they are cooked press the vegetables through a food mill or strainer

Pureed foods to be used in cream soups

Asparagus	Mushrooms
Beans green or wax	Peas
Carrots	Potatoes
Celery	Spinach
Corn	Tomatoes

SHIRRED EGGS

Break 1 egg into a saucer and carefully slide into a well buttered individual baking dish (ramekin) that has been

preheated. Sprinkle lightly with salt and cover with 2 tablespoons of cream. Sprinkle a few buttered bread crumbs over the top and bake in a moderate oven (350° F.) until the white is just set, about 5 minutes.

BROILED OYSTERS
(Yield: 2 servings)

10 to 12 large oysters	2 Tbsp. fine bread or cracker crumbs
1 egg	2 Tbsp. melted butter
[illegible] tsp. salt	

Parsley, if desired

Drain and dry the oysters. Beat egg slightly and add the salt. Dip oysters in egg, roll in crumbs and place on a flat pan. Pour a drop of melted better on each oyster. Broil at high speed until brown (about 1 minute). Turn oysters and pour another drop of butter on each one. Broil this side until brown. Serve at once.

CREAMED CHICKEN
(Yield: 2 servings)

1 cup diced chicken	½ cup medium white sauce (see White Sauce table)
[illegible] cup mushrooms	
1 slice toast	Salt to taste

Mix chicken and mushrooms with hot cream sauce. Serve on a slice of toast. Garnish with parsley, if desired.

BAKED RICE AND CHEESE
(Yield: 6 servings)

[illegible] cup medium white sauce (see White Sauce table)	1 cup rice, uncooked
[illegible] cup grated mild American cheese	[illegible] tsp. salt

EGGNOG

(Yield 1 large glass)

1 egg	1½ tsp sugar
¾ cup milk	¾ tsp vanilla

Pinch of salt

Scald milk in double boiler Pour slowly over well beaten egg stirring constantly Add sugar salt and vanilla Chill thoroughly

SOUPS

Cream soups are desirable for the peptic ulcer patient Soups should not be made with meat stock

(Yield 1 cup)

Add ¼ cup of vegetable puree to the thin white sauce recipe (see White Sauce table page 271) Cook for 20 minutes in a double boiler Stir occasionally If the soup is thicker than desired it may be thinned by adding milk or vegetable water

Puree may be made by cooking fresh frozen or canned vegetables in a small amount of boiling water or in a pressure cooker until tender When they are cooked press the vegetables through a food mill or strainer

Pureed foods to be used in cream soups

Asparagus	Mushrooms
Beans green or wax	Peas
Carrots	Potatoes
Celery	Spinach
Corn	Tomatoes

SHIRRED EGGS

Break 1 egg into a saucer and carefully slide into a well buttered individual baking dish (ramekin) that has been

pan Cook under medium broiler flame 5 minutes or until slightly browned Serve immediately

If no broiler unit is available the bananas may be pan broiled Melt 2 teaspoonfuls of butter in a frying pan on low heat Peel two well ripened bananas and sprinkle each with powdered or brown sugar Cook slowly until slightly browned on one side turn and brown slightly on the other Remove from pan and serve immediately

TABLE FOR WHITE SAUCE
(Yield 1 cup)

Type	*Thin*	*Medium*	*Thick*
Butter	1 Tbsp	1 Tbsp	1 Tbsp
Flour	1 Tbsp	2 Tbsp	3 Tbsp
Milk	1 cup	1 cup	1 cup
Salt	tsp	½ tsp	½ tsp
Used for base of	Cream soups	Creamed vegetables soufflés	Soufflés

Melt butter or margarine add flour and blend thoroughly Scald milk Add scalded milk slowly to butter flour mixture stirring constantly Cook continuing stirring until thick and smooth and there is no starchy flavor Add salt

BAKED CUSTARD
(Yield 2 custards)

1 egg — ¾ cup milk
1 Tbsp sugar — tsp vanilla
tsp salt

Beat egg sugar and salt together Stir in milk and vanilla Pour into custard cups Place in pan of hot water and cook

Cook rice in three cups of rapidly boiling salted water When cooked pour into colander and wash with hot water Add grated cheese to warm white sauce Stir until cheese melts Combine with cooked rice Bake in a buttered casserole (baking dish) in slow oven (325° F) for 20 minutes

ESCALLOPED ASPARAGUS

(Yield 2 servings)

8 asparagus tips (cooked)	2 Tbsp grated cheese
cup medium white sauce (see White Sauce table)	2 tsp bread crumbs

Drain asparagus Arrange in buttered casserole Cover with white sauce Sprinkle cheese and crumbs over the asparagus and white sauce mixture Bake in moderate oven (350 F) about 25 minutes

SPINACH SOUFFLE

(Yield 2 servings)

[illegible] cup thick white sauce (see White Sauce table)	1 egg separated
	tsp salt
[illegible] cup chopped or pureed spinach	[illegible] tsp baking powder

Add chopped or pureed spinach to white sauce Add beaten egg yolk and salt Remove from fire fold in beaten egg white and baking powder Set in pan of hot water and bake 20 minutes in a slow oven (325 F)

BROILED BANANAS

(Yield 2 servings)

Remove the skins from 2 well ripened bananas Spread 1 teaspoonful of butter lightly over each Sprinkle each with 1 teaspoonful of powdered or brown sugar Place in a flat

pan Cook under medium broiler flame 5 minutes or until slightly browned Serve immediately

If no broiler unit is available the bananas may be pan broiled Melt 2 teaspoonfuls of butter in a frying pan on low heat Peel two well ripened bananas and sprinkle each with powdered or brown sugar Cook slowly until slightly browned on one side turn and brown slightly on the other Remove from pan and serve immediately

TABLE FOR WHITE SAUCE
(Yield 1 cup)

Type	*Thin*	*Medium*	*Thick*
Butter	1 Tbsp	1 Tbsp	1 Tbsp
Flour	1 Tbsp	2 Tbsp	3 Tbsp
Milk	1 cup	1 cup	1 cup
Salt	[illegible] tsp	[illegible] tsp	tsp
Used for base of	Cream soups	Creamed vegetables souffles	Souffles

Melt butter or margarine add flour and blend thoroughly Scald milk Add scalded milk slowly to butter flour mixture stirring constantly Cook continuing stirring until thick and smooth and there is no starchy flavor Add salt

BAKED CUSTARD
(Yield 2 custards)

1 egg ¾ cup milk
1 Tbsp sugar tsp vanilla
tsp salt

Beat egg sugar and salt together Stir in milk and vanilla Pour into custard cups Place in pan of hot water and cook

Cook rice in three cups of rapidly boiling salted water When cooked pour into colander and wash with hot water Add grated cheese to warm white sauce Stir until cheese melts Combine with cooked rice Bake in a buttered casserole (baking dish) in slow oven (325 F) for 20 minutes

ESCALLOPED ASPARAGUS

(Yield 2 servings)

8 asparagus tips (cooked)
⅓ cup medium white sauce (see White Sauce table)
2 Tbsp grated cheese
2 tsp bread crumbs

Drain asparagus Arrange in buttered casserole Cover with white sauce Sprinkle cheese and crumbs over the asparagus and white sauce mixture Bake in moderate oven (350 F) about 25 minutes

SPINACH SOUFFLI

(Yield 2 servings)

[illegible] cup thick white sauce (see White Sauce table)
½ cup chopped or pureed spinach
1 egg separated
¼ tsp salt
⅛ tsp baking powder

Add chopped or pureed spinach to white sauce Add beaten egg yolk and salt Remove from fire fold in beaten egg white and baking powder Set in pan of hot water and bake 20 minutes in a slow oven (325° F)

BROILED BANANAS

(Yield 2 servings)

Remove the skins from 2 well ripened bananas Spread 1 teaspoonful of butter lightly over each Sprinkle each with 1 teaspoonful of powdered or brown sugar Place in a flat

pan Cook under medium broiler flame 5 minutes or until slightly browned Serve immediately

If no broiler unit is available the bananas may be pan broiled Melt 2 teaspoonfuls of butter in a frying pan on low heat Peel two well ripened bananas and sprinkle each with powdered or brown sugar Cook slowly until slightly browned on one side turn and brown slightly on the other Remove from pan and serve immediately

TABLE FOR WHITE SAUCE
(Yield 1 cup)

Type	*Thin*	*Medium*	*Thick*
Butter	1 Tbsp	1 Tbsp	1 Tbsp
Flour	1 Tbsp	2 Tbsp	3 Tbsp
Milk	1 cup	1 cup	1 cup
Salt	tsp	[illegible] tsp	tsp
Used for base of	Cream soups	Creamed vegetables souffles	Souffles

Melt butter or margarine add flour and blend thoroughly Scald milk Add scalded milk slowly to butter flour mixture stirring constantly Cook continuing stirring until thick and smooth and there is no starchy flavor Add salt

BAKED CUSTARD
(Yield 2 custards)

1 egg
[illegible] cup milk
1 Tbsp sugar
tsp vanilla
[illegible] tsp salt

Beat egg sugar and salt together Stir in milk and vanilla Pour into custard cups Place in pan of hot water and cook

in a slow oven (325° F) about 25 minutes. To see if the custard is done, insert a knife blade in the custard; if the blade is perfectly clean when removed, the custard is cooked. Canned peaches may be placed in the bottom of the cups and the custard mixture poured over them.

FLOATING ISLANDS
(Yield 2 servings)

1 egg white	[illegible] tsp salt
2 Tbsp powdered sugar	1 recipe of soft custard
¼ tsp vanilla	(see Soft Custard recipe)

Whip egg white until it is stiff but *not* dry. Fold in salt, sugar and vanilla. Drop beaten egg white mixture onto the custard. Place in a slow oven (300° F) until browned. Use one island on each serving of soft custard.

SOFT CUSTARD
(May be served without the Floating Island)

2 egg yolks	1 cup scalded milk
2 Tbsp sugar	[illegible] tsp vanilla
[illegible] tsp salt	

Beat eggs and sugar together. Scald milk in double boiler and pour gradually over egg mixture, beating constantly. Return to double boiler and cook, stirring constantly. Remove custard when it will coat the spoon; add salt and vanilla and allow to cool. Custard will be thin but will thicken on cooling.

Warning: If cooked too long, the custard will curdle. If the water in the double boiler is kept just under the boiling point there will be less likelihood of the mixture curdling.

SPANISH CREAM
(Yield 2 servings)

1 tsp granulated gelatin	1 egg
2 Tbsp cold milk	3 Tbsp sugar
[illegible] cup scalded milk	[illegible] tsp vanilla
[illegible] tsp salt	

Soak gelatin for 5 minutes in cold milk and dissolve in scalded milk Beat egg yolk sugar and salt Stir milk mixture into egg and cook in double boiler until slightly thick Remove from stove and place in cold water till mixture is the consistency of unbeaten egg white Add vanilla Beat egg whites stiff and fold into custard Pour into molds or dessert dishes and chill Serve with whipped cream or peach sauce

RICE BAVARIAN CREAM
(Yield 3 or 4 custards)

2 tsp granulated gelatin	[illegible] cup boiled rice
[illegible] cup cold water	[illegible] tsp salt
[illegible] cup cold milk	[illegible] tsp vanilla
3 Tbsp brown sugar	[illegible] cup whipping cream

Soak gelatin in cold water 5 minutes Scald milk in double boiler stir in gelatin until dissolved Mix sugar rice and salt together add to gelatin mixture Add vanilla and fold whipped cream into *chilled* rice gelatin mixture Mold in cups and serve with whipped cream or peach sauce

FRUIT UPSIDE-DOWN CAKE
(Yield approximately 6 servings)

Peeled fruit either peaches apricots or apples may be used

To prepare pan Butter the bottom of an 8 or 9 inch cake

pan Sprinkle ½ cup brown sugar on the butter Dot the brown sugar lightly with butter or margarine Place the fruit on top of this sugar butter mixture Cover with batter and bake as directed

CAKE RECIPE

3 eggs separated	¼ tsp salt
⅓ cup cold water	1 tsp baking powder
1 cup sugar	1 tsp vanilla
1 cup cake flour	1 tsp lemon extract

Beat the egg yolks and add cold water until the mixture measures about 1 quart Add the sugar gradually Sift flour salt and baking powder together Fold the beaten egg whites gently into the batter mixture Add vanilla and lemon extract Pour into pan prepared for fruit upside down cake Bake in a moderate (350° F) oven 45 minutes or until done To see if the cake is done press it lightly with the finger If the cake springs back into place it is done if there is a dent let the cake cook some more

ZWIEBACK PIE CRUST
(For one 9 inch pie)

1½ cups fine zwieback crumbs ¼ cup confectioner s sugar
6 Tbsp margarine or butter

Melt margarine or butter slowly add sugar and zwieback crumbs combine thoroughly Reserve ½ cup of mixture if desired for top of pie Take remainder and pat firmly into bottom and sides of pie plate Chill as is or bake 5 minutes at 350° F Then cool Fill with cooked filling and cover with meringue or whipped cream and reserved crumbs

LEMON PUDDING

½ cup sugar
¼ cup flour
Dash of salt
1 Tbsp. melted butter
2½ Tbsp. lemon juice
Grated rind of 1 lemon
2 well beaten egg yolks
¾ cup milk, scalded
2 stiffly beaten egg whites

Combine sugar, flour, salt and butter; add lemon juice and rind. Add to combined egg yolks and milk; mix well. Fold in egg whites and pour into greased custard cups. Bake in pan of hot water in moderate oven (350° F.) 45 minutes. When baked, each dessert will have custard on the bottom and sponge cake on top. Serves 4.

BROWN BETTY

3 Tbsp. melted butter or margarine
1½ cups bread crumbs
4 large apples
½ cup brown sugar
½ tsp. ground cinnamon
¼ tsp. grated nutmeg
1 tsp. lemon juice
[illegible] cup hot water

Mix together melted butter and freshly ground bread crumbs. Sprinkle half the buttered crumbs on the bottom of a baking dish. Combine sugar and spices with apples which have been peeled, cored and sliced. Place this mixture over crumbs in baking dish. Pour over all the lemon juice and hot water. Sprinkle the remaining buttered crumbs over the top and cover the baking dish. Bake in moderate oven (350° F.) 25 minutes; uncover and continue baking 20 minutes longer. Serve with whipped cream or thick sour cream. Serves 4.

APRICOT FLIP

3 canned apricot halves
3 tbsp. apricot nectar
¾ cup chilled milk
1 tsp. sugar
¼ cup heavy cream, chilled
1 or 2 drops almond extract

Slice apricot halves and put them with their syrup (nectar) and the milk in a chilled Waring Blendor. Run blender until fruit becomes a puree. Add sugar, cream, and extract and blend for another 2 seconds. Pour into a tall glass which has been chilled.

PUMPKIN CUSTARD
(Yield: 4 servings)

2 cups milk	*3 well-beaten eggs*
1 Tbsp. butter	½ cup light brown sugar
1 cup cooked strained pumpkin	½ tsp. salt
	1 tsp. vanilla extract

Cinnamon

Scald the milk, add all the ingredients except the cinnamon. Turn into a buttered baking dish, set in a pan of hot water, and bake in a moderate oven (350° F.) 45 minutes or until a silver knife comes out clean when inserted in the middle of the custard. Dust lightly with cinnamon and serve with cream.

EGGS VIENNA STYLE

½ cup light cream	2 eggs
Salt	2 slices crusted white toast

2 slices crisp bacon

Bring cream to a boil, add a dash of salt, and carefully poach the eggs in the cream. Cut each slice of toast into four pieces and assemble on a hot dinner plate. Place an egg on each slice of toast, and slowly pour the cream over all so that the toast absorbs all the liquid. Have crisp bacon crumbled into small pieces, and sprinkle these over the eggs and toast. Serve at once.

SAMPLE MENUS FOR ONE WEEK OF AMBULATORY STAGE MANAGEMENT

Breakfast	*Luncheon*	*Dinner*
3 oz strained orange juice dil with 3 oz warm water Cornflakes with sliced ripe banana Cream and sugar Soft cooked egg White toast butter Sanka	Cream of mushroom soup salt-ines Toasted Philadelphia cream cheese sandwich Sliced Raggedy Ann peaches and Holland wafers Milk	Blended fruit juice (apricot pineapple grapefruit juice) Roast rib of beef Mashed potato with butter Pureed beets Baked Roman Beauty apple (without skin) Melba toast butter Milk
Canned pear half in natural syrup Cream of Wheat with finely chopped dates Cream and sugar Crisp bacon White toast butter Sanka	Tomato juice dil [illegible] with water Broiled beef patty on Kaiser hard roll butter Buttered asparagus tips Baked custard with cream Milk	Cream of carrot soup Broiled breast of chicken Buttered rice with finely chopped parsley Whipped acorn squash Peeled Italian plums vanilla wafers Melba toast or saltines butter Milk

Slice apricot halves and put them with their syrup (nectar) and the milk in a chilled Waring Blendor Run blender until fruit becomes a puree Add sugar cream and extract and blend for another 2 seconds Pour into a tall glass which has been chilled

PUMPKIN CUSTARD
(Yield 4 servings)

2 cups milk	3 well beaten eggs
1 Tbsp butter	½ cup light brown sugar
1 cup cooked strained pumpkin	½ tsp salt
	1 tsp vanilla extract

Cinnamon

Scald the milk add all the ingredients except the cinnamon Turn into a buttered baking dish set in a pan of hot water and bake in a moderate oven (350 F) 45 minutes or until a silver knife comes out clean when inserted in the middle of the custard Dust lightly with cinnamon and serve with cream

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Salt	2 slices crusted white toast

2 slices crisp bacon

Bring cream to a boil add a dash of salt and carefully poach the eggs in the cream Cut each slice of toast into four pieces and assemble on a hot dinner plate Place an egg on each slice of toast and slowly pour the cream over all so that the toast absorbs all the liquid Have crisp bacon crumbled into small pieces and sprinkle these over the eggs and toast Serve at once

Strained oatmeal cream and sugar 2 *poached eggs* on buttered white toast Crisp bacon Sanka	*[illegible] an cheese* Lemon pudding Melba toast butter Milk	Purée of beets Brown Betty *Hard French roll* butter Milk
3 oz. strained pineapple juice diluted with 3 oz. warm water Rice Krispies *with sliced banana* cream and sugar Eggs Vienna style Sanka	Toasted chicken sandwich on *white bread* butter Molded cherries (Bing and Royal Anne) in raspberry Jello Cheesecake (no raisins)	Broiled steak Parsleyed buttered potato Puree of carrots Melba toast *butter* Boston cream pie
Baked Roman Beauty apple (without skin) cream Farina cream and sugar Shirred eggs White toast butter Sanka	Cream of pea soup Peach and pear halves with *cottage cheese* Buttered saltines Maple junket cream Angelfood square Milk	Blended fruit juice (*grape apricot* strained orange juice) Roast leg of lamb Escalloped potatoes Buttered *asparagus tips* Pumpkin custard Milk

Breakfast	*Luncheon*	*Dinner*
3 oz sweetened grapefruit juice dil with 3 oz warm water Soft scrambled eggs Crisp bacon White toast butter Sanka	Roast beef sandwich on white bread butter Whole peeled apricots molded in lime Jello Floating Island Milk	Apple juice Broiled lamb chop Baked potato with butter Puree of green beans Fruit compote sliced ripe banana Royal Anne cherries sliced peaches Sponge cake square Melba toast or saltines butter Milk
Fresh apple sauce with cream Bacon omelet White toast butter Sanka	Creamed sweetbreads and chopped mushrooms on Holland rusk Puree of peas Orange sherbet vanilla wafers Milk	Baked halibut with Mornay sauce Whipped potatoes Puree of spinach with lemon Chocolate blancmange Melba toast or saltines butter Milk
3 oz strained orange juice dil with 3 oz warm water	Tomato juice dil with water Baked macaroni and mild Amer	Broiled calves liver Double baked potato

Strained oatmeal cream and sugar 2 poached eggs on buttered white toast Crisp bacon Sanka	ican cheese Lemon pudding Melba toast butter Milk	Puree of beets Brown Betty Hard French roll butter Milk
3 oz strained pineapple juice dil with 3 oz warm water Rice Krispies with sliced banana cream and sugar Eggs Vienna style Sanka	Toasted chicken sandwich on white bread butter Molded cherries (Bing and Royal Anne) in raspberry Jello Cheesecake (no raisins)	Broiled steak Parsleyed buttered potato Puree of carrots Melba toast butter Boston cream pie
Baked Roman Beauty apple (without skin) cream Farina cream and sugar Shirred eggs White toast butter Sanka	Cream of pea soup Peach and pear halves with cottage cheese Buttered saltines Maple junket cream Angelfood square Milk	Blended fruit juice (grape apricot strained orange juice) Roast leg of lamb Escalloped potatoes Buttered asparagus tips Pumpkin custard Milk

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